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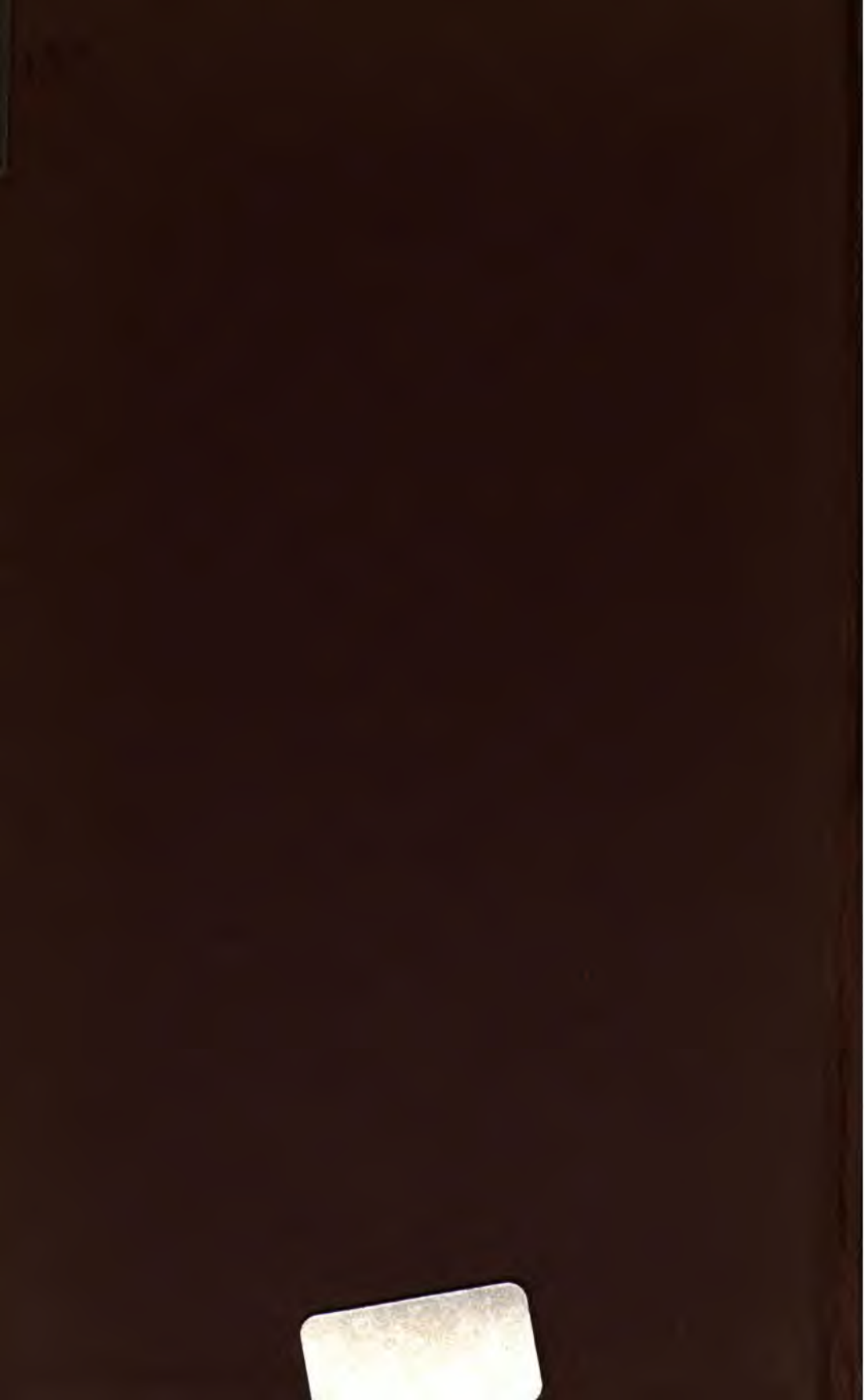

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A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS

IN THE

MEDICAL AND SURGICAL SCIENCES.

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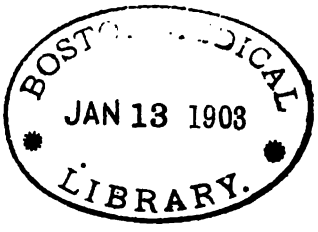

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PROGRESSIVE MEDICINE.

DECEMBER, 1902.

DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER, PANCREAS, AND PERITONEUM.

By MAX EINHORN, M.D.

THE MOUTH AND TONGUE.

Stomatitis Ulcerosa Chronica. Forchheimer[1] is in favor of giving the name stomatitis ulcerosa chronica to that disease of the gums and mouth usually known as pyorrhœa alveolaris. Concerning its etiology, he believes that it is always caused by poison excreted by the salivary glands, as mercury, phosphorus, or lead-poisoning. In a similar way certain organic toxins may act, as the toxin of measles, the toxins of a large number of acute infectious diseases; possibly the ptomaïnes, as in scurvy; and, lastly, such bodies as the aloxurs, which finally lead to the formation of uric acid. Regarding treatment, each patient should be attended both locally by the dentist and constitutionally by the physician; in the latter case the treatment should, of course, be directed against the etiological factor of the disease.

Black Tongue. George Reinecke[2] describes seven cases of black tongue. In this condition the surface of the tongue presents a dark, black, or brownish, rarely green, color. Usually this discoloration involves only the anterior part of the tongue, extending to the papillæ circumvallatæ. This disease appears in an acute and chronic form, and is due to a certain kind of mould, producing a dark color.

Pruritus Senilis Linguæ. Two cases of a peculiar affection of the tongue, which he calls pruritus senilis linguæ, have been observed by Baumgarten.[3] He considers the affection a manifestation of the ordi-

[1] St. Paul Medical Journal, June, 1901.
[2] Deutsche Archiv f. klin. Med., 1901, p. 575.
[3] Münchener med. Wochenschrift, 1901, No. 39.

nary pruritus senilis of the skin, as he could find no other cause for it. Treatment was absolutely unsuccessful.

Noma. Fischer[1] reports a case of noma of the right cheek following scarlatina. The ulceration got well after the use of the Paquelin cautery and the application of an ointment consisting of equal parts of lanolin and ichthyol.

Fishbone in the Throat. Breitung,[2] in describing the removal of a fishbone from the throat, lays stress upon two important points, viz.:

1. The seat of the fishbone is usually referred much lower down by the patient than it actually is.

2. Palpation by means of the finger is of great value and often will discover the foreign body where everything else fails.

THE ŒSOPHAGUS.

Œsophagoscopy. Œsophagoscopy in the diseases of the œsophagus and cardia has gained an important place in the last few years. All the literature of importance on this subject will be found in an article[3] published by me in the year 1897 regarding the inspection of the œsophagus and cardia. Further important papers on œsophagoscopy are those of von Hacker[4] and Rosenheim.[5] Von Hacker's epoch-making labors show clearly the high and practical value of this method of examination, which not only facilitates the diagnosis of many of the diseases of the œsophagus, but frequently exerts a direct influence upon their treatment.

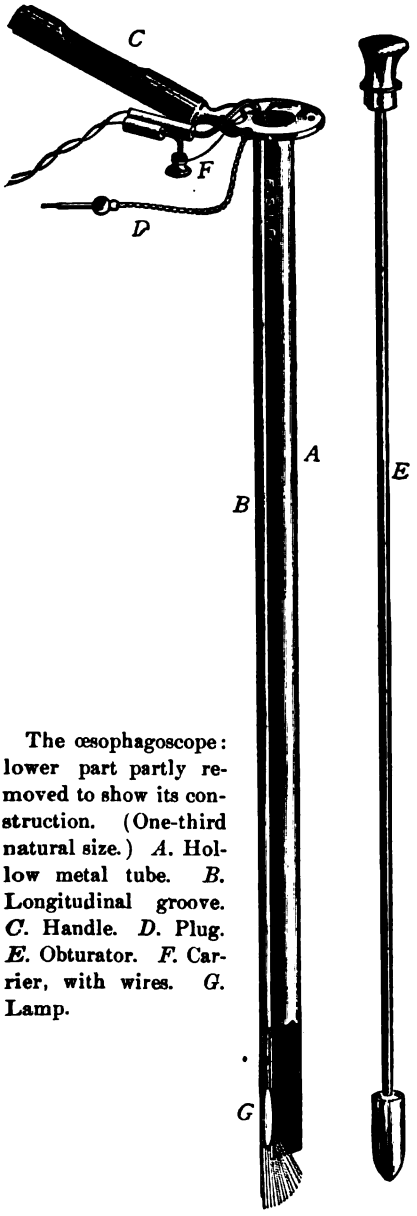
In the instruments used up to now for œsophagoscopy (Mikulicz, Rosenheim, Kelling) the source of the illumination is outside of the œsophageal tube. As a rule, the panelectroscope is employed for this purpose—an instrument which throws concentrated light through the whole tube, thus illuminating the lowest spot that is to be inspected. It is evident that inspection would be easier if the lamp were placed at the lower end of the tube, near the area to be examined, since a better illumination could in this way be secured. With the appearance of the so-called "cold lamps" this principle could be practically executed.

The œsophagoscope which I[6] use consists, as the accompanying drawing (Fig. 1) illustrates, of a round, hollow metal tube (*A*), having on one side a small longitudinal groove (*B*), which is separated by a thin

[1] American Journal of the Medical Sciences, April, 1902, p. 643.
[2] Münchener med. Wochenschrift, 1901, No. 28.
[3] New York Medical Journal, December 11, 1897.
[4] Beiträge zur klinischen Chirurgie, 1898, Band xx. p. 141. Ibid., p. 275. Ibid., 1901, Band xxix. p. 128.
[5] Deutsche Klinik, 1901.
[6] Medical Record, January 25, 1902.

wall from the lumen of the tube. Two isolated electric wires attached to a carrier (*F*) run through the groove (*B*). The carrier can be easily

Fig. 1.



The œsophagoscope: lower part partly removed to show its construction. (One-third natural size.) *A*. Hollow metal tube. *B*. Longitudinal groove. *C*. Handle. *D*. Plug. *E*. Obturator. *F*. Carrier, with wires. *G*. Lamp.

Fig. 2.

Showing patient with œsophagoscope inserted ready for inspection.

removed with the lamp, thus facilitating thorough cleansing and sterilization of the instrument and any necessary renewal of lamp. At their end a small lamp (*G*) is attached and placed a little above the end opening of tube (*A*), being, however, not inclosed by the thin metal sheet that covers the wires. To the tube is attached a handle (*C*), a plug (*D*), and an obturator (*E*). Before introducing the instrument the obturator must be in place, and is held there firmly by means of the plug (*D*). After the introduction of the instrument this plug is removed and the obturator withdrawn. The wires are connected with an electric battery, and everything is now ready for inspection. The

handle (*C*) facilitates the use of the instrument. I usually practice œsophagoscopy in the sitting posture, without any anæsthetic (cocaine spray, etc.). The procedure is not a difficult one, and is done as follows:

Method. The patient sits on a chair which has a back. The instrument (with obturator inserted) is immersed in warm water, and, while depressing the tongue with the left index finger, is held in the right hand like a pen and introduced into the mouth and pharynx of the patient. The latter is now directed to throw his head backward and the instrument is then pushed down into the œsophagus without exerting any force.

The accompanying drawing (Fig. 2) shows the position of the patient after the introduction of the instrument. Attention must be paid that the lips of the patient are not pressed by the instrument. The obturator is now removed, the connection made; an inspection may then take place by looking into the tube. At the end of this the mucous membrane of the œsophagus is plainly visible. If the instrument is slowly withdrawn while looking into it, the whole wall of the œsophagus may thus be inspected.

I have had the œsophagoscope made in two different lengths (35 and 40 cm.) and thicknesses (1 and 1½ cm.), which will fulfil various indications. The thicker instrument will be used more especially in the local application of medicaments or for the removal of foreign bodies, whereas we would ordinarily get along with the more slender instrument.

Kelling[1] likewise advocates strongly the use of the œsophagoscope and the gastroscope. He claims especial advantage in the diagnosis of carcinoma of the œsophagus and stomach, not considering even its wide possibilities in removing foreign bodies from the œsophagus, etc. He thinks that gastroscopy ought to a certain degree supplant or prevent exploratory laparotomies for carcinoma of the stomach. He claims for his method its safety and convenience as against exploratory laparotomy. Finally he describes a method of inflating the free peritoneal cavity with air, and through a trocar examining the surfaces of the liver, gall-bladder, stomach, etc., by means of a fine Nitze cystoscope.

Diverticulum of the Œsophagus. Mayr and Dehler[2] relate the case of a man suffering from a diverticulum of the œsophagus, situated 10 cm. from the teeth. Internal treatment being of no avail, operative interference was decided upon. The diverticulum was removed from the right side of the throat, the opening in the œsophagus sutured, and the wound left open. Everything healed satisfactorily without any

[1] Münchener med. Wochenschrift, 1902, No. 1.
[2] Ibid., 1901, No. 37.

leakage from the œsophagus. The results of a microscopic examination of the sac are also given.

The Diagnosis of Deep-seated Diverticula of the Œsophagus. W. Zweig[1] employs the following procedure for differentiating between idiopathic dilatation of the œsophagus and a deep-seated diverticulum of this canal. He first introduces a tube provided with a funnel into the sacculated area of the œsophagus, then inserts a similar apparatus into the gastric cavity. Through the first tube about 100 c.c. of a methylene blue solution is poured into the œsophagus, and then the gastric tube is withdrawn. If the tube returns without any color, we have to deal with a diverticulum; if it is stained with methylene blue, then the affection in question is a dilated œsophagus. By means of this simple manœuvre Zweig was enabled to diagnose a deep-seated diverticulum in three cases.

Idiopathic Dilatation of the Œsophagus. A number of cases of idiopathic dilatation of the œsophagus have been reported by Theodore Rosenheim.[2] According to his opinion, the swallowing sound is not of much value in this affection. I must say, however, that I consider absence of the swallowing sound as one of the most important signs in the diagnosis of this disease. In twelve cases of idiopathic dilatation of the œsophagus I have personally treated the swallowing sound was always absent. With regard to treatment, Rosenheim recommends, especially for cases in which there exists a spasm at the cardia, dilatation of this orifice from the stomach. This is done by introducing into the gastric cavity a thin tube to which is attached an inflatable balloon, filling up the balloon with air and then dragging it forcibly through the cardia.

Cahen[3] gives a detailed history of a patient suffering from spasm of the cardia, with subsequent dilatation of the œsophagus and inability to force food into the stomach. The patient was finally operated on and a gastric fistula established according to the method of Witzel. About a month later retrograde dilatation of the cardia was begun by means of permanent bougies. There was at first some difficulty in passing the silk thread, but the attempts were finally successful after having enlarged the fistula by means of a nitrate of silver stick. By means of the thread, bougies were drawn through the cardia from the stomach and left in the œsophagus, at first two to three hours, but later for twenty-four hours. With this was combined thorough irrigation and drainage of the dilated œsophagus. The result was very good, the patient being again enabled to eat and drink, only occasionally (every ten to fourteen days) resorting to the stomach-tube in order to cleanse the œsophagus.

[1] Deutsche med. Wochenschrift, 1901, No. 33.
[2] Berliner klin. Wochenschrift, 1902, Nos. 11, 12, and 13.
[3] Münchener med. Wochenschrift, No. 11.

THE STOMACH.

Testing the Acidity of the Gastric Contents. The amount of HCl, and in most instances also that of the total acidity, can be approximately gauged[1] by means of a strip of paper saturated with a ½ per cent. dimethylamido-azo-benzol-solution aided by dilution. The procedure is as follows:

A minute quantity of stomach contents is placed by means of a glass rod upon a strip of dimethylamido-azo-benzol paper (½ by 8 centimetres). If the paper turns red, one drop of the contents is diluted with two drops of water in a small porcelain dish. A glass rod is dipped into the mixture and the test-paper again touched. If it still turns red, one or two more drops of water are added and the procedure repeated as before. This is done until only a slightly red or almost no red color is produced by the mixture upon the test-paper. In this way the amount of dilution required for a trace reaction with the test-paper is determined. It is clear that the more HCl there is in the stomach contents the more they can be diluted, still giving a trace reaction with the dimethylamido-azo-benzol paper. A dilution of from 3 to 6 would correspond to a normal, under 3 to a subnormal acidity, and over 6 to hyperacidity.

The numbers given refer to the examination one to one and one-half hours after Ewald's test-breakfast. If we have to test after other more complicated meals (test dinner, etc.) hyperacidity would be indicated by somewhat smaller amounts of dilution (from about six times on), since we estimate approximately only the free HCl, and the amount of the latter is relatively small after meals containing much albumin.

The method just described of approximately determining the quantity of free HCl in the stomach contents will be of value in the following two conditions: (1) In examinations with the stomach bucket, or where from other causes only small quantities of gastric contents are at our disposal; (2) in cases in which it is of importance to obtain at once an idea regarding the amount of acidity and the necessary solutions for titration are not at hand.

A new method of testing the acidity of the stomach contents has been devised by E. K. Dunham.[2] It consists in having the patient swallow a thread colored with litmus, congo, or dimethylamido-azo-benzol.

Thirty inches of thread, with a small tassel attached to the end, can be swallowed with from 10 to 30 cubic centimetres of water—a quantity

[1] Medical News, July 20, 1901.

[2] New York University Bulletin of the Medical Sciences, October, 1901, vol. i., No. 4, p. 178.

too small to greatly dilute the contents of the stomach and probably not sufficient to materially modify qualitative tests.

The apparatus required is very simple—a thread, preferably of silk, a cylindrical reel of wood about half an inch in diameter, a glass tube of small calibre, and a small tassel of test-threads colored with the desired indicators. The tassel is tied to one end of the thread, is then passed through the glass tube, tied to and then wound upon the reel, the tassel being made to just engage in the opening of the tube. This reel is then floated upon water in a glass, the tassel end of the tube placed well over the arch of the tongue, and the water drunk through the tube in small, quick swallows. The end of the tube which dips into the water should be kept well below the level of the reel, otherwise the thread, in passing into the tube, will draw the reel against the end of the tube and cause too much friction. When the act of swallowing has unwound all the thread on the reel the free end is detached from the reel and the tube removed from the mouth. The thread should not be withdrawn from the stomach in less than three minutes, and it is better to let it remain there for five minutes. After removal it should not be washed lest the original color return to the threads dyed with dimethylamido-azo-benzol.

Determination of the Amount of Pepsin. Jung[1] analyzes the recent investigations of Pawlow on the work of the digestive glands, and then enters upon a comparison of Metts' and Hammerschlag's methods of estimating the amount of pepsin. He finds Metts' a more accurate and reliable method than Hammerschlag's. With Metts' method subacidity and anacidity have lower pepsin values than normal or superacidity. Superacidity, generally speaking, has the highest values of pepsin.

Metts' method consists in measuring the amount of albumin digested in a small 3 cm. glass tube during ten hours' exposure to the gastric juice.

Arrangement to Prevent Clogging of the Tube. Clemm[2] has constructed a new appliance, which is supposed to prevent clogging, by means of food particles, of the openings in a stomach-tube. It consists of a thin, flexible copper wire, at the end of which is attached a small basket-like appliance which closely fits the lumen of the tube, and is provided with two lateral sharp cutting surfaces that will disintegrate the toughest particles of food. The stomach-tube itself is V-shaped at its upper end, one side being connected with a funnel, the other serving to hold the handle of the cutting mandril.

[1] Journal of American Medical Association, May 10, 1902.
[2] Münchener med. Wochenschrift, 1901, No. 50.

Examination of the Gastric Functions. F. Seiler[1] tested a new method, suggested by Sahli, for the examination of the gastric functions. The principle of the new method consists in administering a test-meal containing some fat in emulsion in conjunction with some other food. After a certain time a sample of gastric contents is obtained and the amount of fat as well as the acidity is determined. In so far as the fat does not change in the stomach, its percentage may serve as an indicator for the amount of food left in the stomach. If, now, the amount of fluid in the stomach at the time of examination is ascertained after the method of Rémond and Mathieu, the actual amount of gastric secretion can be easily figured. The test-meal of Sahli consists of a flour soup prepared with butter. The determination of the percentage of fat is quite complicated, and this makes the method impracticable.

The Influence of Drugs on the Gastric Functions. Boardman Reed[2] has undertaken as experimental study with regard to the condition of the gastric functions in five healthy individuals when treated with different drugs. He arrived at the following conclusions:

1. Perfectly normal stomachs are probably in the minority in large cities, especially among persons employed indoors.

2. In stomachs which are normal, or approximately so, the digestion may be injured by a simple bitter tonic, taken even for a short time.

3. Quite moderate doses of HCl administered as a medicine may prove effective in hypochlorhydria, but are likely to do harm to normal stomachs and certain to aggravate hyperchlorhydria.

4. Pepsin rarely produces any good result when given alone, even to persons with weak digestive power, and often then retards the digestion of albuminoids.

5. Pepsin and HCl given together much more frequently do good than either administered singly.

Action of the Saliva. As the result of a series of experiments Hensay[3] finds that the function of the saliva is not principally a physical one, but that the chemical function is of especial importance and value. In his experiments large amounts of starch, larger in fact than was expected, were found to have been changed by the saliva.

The Influence of Retention of Bile on Gastric Secretion. S. Simnitzky[4] has made the observation that in cases of retention of bile (icterus) there is increased secretion of gastric juice, or hyperchlorhydria. As soon as the bile flows freely into the intestinal canal the hyperacidity ceases. He could prove the same condition experi-

[1] Deutsche Arch. f. klin. Med., 1901, p. 271.
[2] Journal of American Medical Association, January 11, 1902.
[3] Münchener med. Wochenschrift, 1901, No. 30.
[4] Berliner klin. Wochenschrift, 1901, No. 43.

mentally in animals. This cannot be taken as a strict law, as I have frequently observed cases of jaundice with normal and even diminished gastric secretion.

Action of Alcohol Enemata on Gastric Secretion. Spiro[1] gives the results of some experiments with rectal enemata of alcohol upon the secretion of the stomach. For this purpose he used clysmata of absolute alcohol, brandy, white wine, claret, and bottled beer suspended in physiological salt solution. He concludes that:

1. Absolute alcohol and alcoholic drinks given per rectum excite the secretion of gastric juice.

2. The effects are seen after the use of 7 to 10 c.c. absolute alcohol or its equivalent in beverages.

3. The highest acidity is found one hour after the injection, decreasing gradually thereafter.

4. In cases of achylia, as well as of carcinoma of the stomach, a result from the use of alcohol enemata was not observed.

Effect of Carbonic Acid on Gastric Digestion. The action of carbonic acid gas on gastric digestion has been studied by F. Penzoldt.[2] In carrying out his experiments he used the ordinary mineral waters charged with the gas. He found that it accelerates the hydrochloric acid secretion in the stomach, and also increases the motor function, an ordinary meal leaving the stomach in a somewhat shorter period of time than normally. Penzoldt, therefore, recommends the use of mineral water in gastric affections, excepting in ulcerative processes and obstructions of the pylorus.

Gastric Secretion in Chronic Rheumatism. Frank H. Murdoch[3] has examined six cases of chronic rheumatism with regard to the condition of gastric secretion, and in most of his cases found the gastric juice not far from normal. Murdoch believes that strict attention toward improving digestive difficulties will be of great value in the amelioration of the rheumatic condition.

Difficulty of Diagnosis in Gastro-intestinal Disorders. H. W. Bettmann[4] reports several cases of gastro-intestinal disorders in which it was easy to be led astray by the prevailing symptoms. He describes cases of chronic diarrhœa in which the underlying factor was constipation. It is not uncommon for small masses of fecal matter to lodge in the large bowel and set up an irritation which may persist for weeks or months. After an erosion of the mucous membrane has occurred the bowel contents may prevent a return to health, even under careful

[1] Münchener med. Wochenschrift, 1901, No. 47.
[2] Deutsche Arch. f. klin. Med., 1902, p. 200.
[3] Medical News, August 3, 1901.
[4] Cincinnati Lancet-Clinic, June 23, 1900.

management, unless the cause of the trouble is luckily hit upon. The seat of such erosion is more commonly the cæcum or the descending colon or sigmoid, and the diagnosis in such cases is easy. But when the transverse colon is affected the seat of the pain and the reflex gastric symptoms may readily lead to the greatest confusion. Under such circumstances we can make a correct diagnosis only by a careful study of the gastric functions and secretions, and by thus gradually excluding the stomach from the clinical picture. Pain in the region of the umbilicus, when otherwise not explicable, is always suspicious of rectal disease, and by keeping this fact in mind we may often be put on the right track of an otherwise obscure condition.

It is easy to mistake hepatic for gastric disorders, and *vice versa*, and the right kidney very often leads to symptoms very similar to those produced by diseases of the liver or stomach. A movable right kidney may occasionally produce violent gastric symptoms similar in nearly all respects to a primary gastric crisis. It is usually the slighter symptoms, however, which lead to error, because they seldom lead to as careful an examination as the more severe attacks. Intensity of suffering is sometimes a great advantage to the patient, inasmuch as it often induces the attending physician to study the underlying conditions more closely.

A smart attack of gallstone colic often clears up a diagnosis about which doubt may have hovered.

One of the most perplexing practical problems in internal medicine s to interpret correctly the various forms of pain and pressure in the stomach. Gastralgia, a term which at one time was supposed to mean much, now means very little; and some clinicians have even denied the existence of a neuralgia of the stomach, ascribing all such pains to the presence of gallstones. Certain it is that gallstones may manifest themselves for months or years in no other way than by producing attacks of gastralgia. Gallstones may set up various forms of gastric disturbances without revealing their presence by localized symptoms of any kind, and we are greatly in need of a method of diagnosing gallstones before colic, jaundice, or local tenderness reveals their existence to us.

Relation between Dyspeptic Conditions and Affections of the Female Genital Organs. A. Sommer[1] has examined a great number of women, principally with retroflexed uteri, with regard to the condition of the stomach. He frequently found gastroptosis and hyperchlorhydria present, but does not believe that the stomach trouble was due to the uterine disorder.

[1] Centralblatt f. innere Medicin, March 1, 1902.

Diet. In speaking of diet in diseases of the stomach and intestines, Schmidt[1] believes that the principal chemical function of the stomach consists in separating the food chemically into small particles, and to a less degree of bringing the food into a readily absorbable state. He is of the opinion that all dieting has the fundamental object of reducing the amount of work performed by the stomach. For this reason all food should be introduced as finely subdivided as possible. The article of diet most difficult to disintegrate by the stomach is meat, and above all, raw and smoked meat. Examination of the stools in anacidity very often will reveal the presence of connective-tissue shreds, pieces of ham, etc. The advantages of raw meat are the stimulus it exerts on the production of gastric juice and its ability of entering into combination with relatively large amounts of free HCl. The latter effect is also produced by the meat extracts, and it is, therefore, preferable to use them rather than raw meat in all cases of subacidity where we wish to stimulate the flow of gastric juice. In hyperacidity also, with the idea of giving the stomach as much rest as possible, Schmidt discards the use of raw meat as far as possible. For hyperacidity he believes an amylaceous diet the best.

In the dietetic treatment of intestinal diseases it is of great importance in all cases of irritation to give the food finely subdivided. Of two articles of food of equal nutritive value the one is to be preferred which requires the least chemical change during digestion. At the head of the list of easily digestible foods is milk. If this causes constipation or diarrhœa the addition of 0.25 to 0.5 gramme of salicylic acid to 1½ to 2 litres of milk will often overcome the difficulty. He also recommends fat (butter) in the treatment of enteric disorders.

THE DIETARY REGIMEN IN CHRONIC AFFECTIONS OF THE HEART. H. Illoway[2] discusses this subject at length and gives the following rules:

1. *As to Foods.* (*a*) All foods that have bulk must be excluded. (*b*) All foods that are flatulent must be excluded. (*c*) Only foods that are readily and easily digestible are allowed. (*d*) All foods must be so cooked that their digestion is facilitated thereby, not impeded.

2. *As to Meals.* (*a*) All meals shall be small, so that the stomach is not taxed too much or greatly distended. (*b*) The intervals between the meals must be so regulated that sufficient time is given the stomach to empty itself and to have an interval of rest before the next meal is taken.

Artificial Foods. In a study of artificial foods Hoppe[3] finds that the three principal substitutes, roborat, plasmon, and tropon, are utilized

[1] Münchener med. Wochenschrift, 1902, Nos. 6 and 7.
[2] American Journal of the Medical Sciences, March, 1902, p. 457.
[3] Münchener med. Wochenschrift, No. 12.

to a large extent (about 95 per cent.) in the body. For artificial feeding per rectum, plasmon in 25 per cent. solution is the most suitable. He also determined that roborat diminishes the formation in the body of uric acid, and also the excretion of chlorides in the urine.

Brat[1] describes some experiments made with a new food preparation, gluton, a derivative of gelatin. He comes to the conclusion that gluton is utilized in the body to the same extent as other albuminous food-stuffs, and that it possesses the same nutritive value as gelatin, but that it has the advantage of permitting the use of larger amounts than can be given of gelatin.

He thinks that it would be indicated in obesity to preserve the albumin of the body, in diabetes, in fever, and, perhaps, in hemorrhage.

An examination of various artificial food-stuffs, among them plasmon, soson, fersan, roborat, and others was made by Weissbein.[2] He employed a method of color analysis to determine the composition of the various preparations. For this purpose he made use of Pappenheim's modification of the Ehrlich triacid stain, which will differentially stain all albuminous substances. For the starchy bodies he used iodine. In his examinations he arrived at his conclusions by means of these two solutions, a centrifuge and a microscope.

The Origin of Fat. Rosenfeld,[3] after agreeing with Pflüger that fat is never produced from albuminous substances but only from fat or carbohydrates, proceeds to analyze the origin and modifications of the different varieties of fat in domestic and marine animals. Regarding the "urfett," the first original fat, he thinks that it was synthetically compounded by means of plants, either in the form of carbohydrates which could be transformed into fat by all animals, or, perhaps, in the form of fat itself.

The Action of Pancreon. Loeb[4] publishes the results obtained with pancreon (a form of pancreatin) in thirteen cases of achylia gastrica. The idea of giving the preparation in these cases was to aid the weak or rather functionally inadequate stomach in producing a chyme that would be less irritating to the intestine. Four of the cases suffered from diarrhœa, seven from constipation, and two were normal. As a result of his treatment he had undoubted success in nine cases, relieving the subjective complaints as well as objectively the bowel disturbances, either diarrhœa or constipation. In two cases a return of free HCl could be demonstrated.

The Abuse of Coffee. While in moderate quantity coffee is one of the best stimulants we possess, if taken in larger amounts it frequently

[1] Deutsche med. Wochenschrift, 1902, No. 2.
[2] Ibid.
[3] Münchener med. Wochenschrift, 1902, No. 1.
[4] Ibid., 1901, No. 31.

causes disagreeable symptoms. W. M. Leszynsky[1] has recently written an important paper on the deleterious effects of this beverage.

Victims of the coffee habit usually complain of the following symptoms, which are more or less pronounced, and in varying combination: General headache and "nervousness;" apprehension in regard to some unknown impending trouble; mental depression and irritability; insomnia or restless sleep; "bad dreams;" sudden "starting" in sleep and awaking in profuse perspiration; occasional or frequent vertigo; general tremulousness and diminished muscular power; precordial oppression; cardiac palpitation; loss of appetite; frequent eructation of gas, and constipation. The symptom-complex most commonly noted is: general nervousness; tremor; vertigo; restless sleep; cardiac palpitation; eructation of gas, and constipation. On examination we usually find a coated and tremulous tongue; tremor in the eyelids while standing with closed eyes; in some the pupils are slightly dilated, but react quickly to light; tremor in both outstretched hands; rapid pulse, of low tension and frequently irregular, ranging from 90 to 130; exaggerated reflexes, and more or less increased reflex irritability. Tachycardia or bradycardia may also be present.

In the treatment of these patients Leszynsky does not recommend immediate and total abstinence. As a general rule, their allowance should at once be limited to one cup of coffee in the morning. If necessary its strength should be gradually reduced or its use absolutely prohibited. The customary stimulant being suddenly withdrawn, if careful instructions are not given the patient will soon find a substitute in tea or cocoa, or possibly alcohol. An infusion of cocoa-nibs in moderate quantity frequently proves acceptable in place of coffee. There are many preparations on the market under various names, and generally advertised as "substitutes for coffee." They are known to contain parched corn, peas, beans, and corn-cobs, as well as sweet potatoes cut into small pieces, dried and parched. Chicory is commonly used mixed with true coffee. The manufacturers of more recently vaunted substitutes claim that their special preparations are made of cereals. Leszynsky has long since refrained from recommending any of them, as their continued use soon leads to disturbance of digestion. While cocoa possesses considerable nutritive value, its principal alkaloid is theobromine, which is almost identical with caffeine in its chemical and physiological effects. With but slight qualifications the same may be said of tea and its alkaloid theine. Hence the use of cocoa and tea must be restricted or forbidden. Suitable hydriatic treatment and careful attention to the diet and excretions should be systematically

[1] Medical Record, January 12, 1901.

carried out. In some cases it may be necessary to institute a "rest cure."

As a sedative to the nervous system, and also temporarily to replace the accustomed stimulation, it has been Leszynsky's routine practice to prescribe the following mixture, to be taken in water three times a day:

℞.—Sodii bromidi	gr. xv.
Liq. potassii arsenitis	♏ij.
Tinct. gentian. comp.	f℥ss.
Ext. kola fl.	♏xv.—M.

At the end of five or six weeks the bromide, etc., should be discontinued, and tonic pills containing arsenic, quinine, and strychnine, or some similar combination, taken daily for several months. Under the foregoing plan of treatment, faithfully followed, most of these patients will completely recover within three to six months.

Gastro-intestinal Diseases Causing Anæmia. McCaskey[1] gives the histories of two patients in whom a severe anæmia was secondary to gastro-intestinal disease, and who were cured by treating the gastro-intestinal trouble.

Regarding the causation of this secondary anæmia we should recognize: (1) The importance of varying grades of subnutrition; (2) the chemical factor as a factor in morbid hæmogenesis; and (3) that intangible something, the expression of a hereditary or acquired vice, which determines what has been called the vulnerability of the tissue or organ.

The Role of Heredity in Digestive Diseases. The influence of heredity in gastro-enteric disturbances has been studied by Jung.[2] From statistical data relating to this question he concluded that one family out of every two presents more than one case of digestive disturbance of the same nature.

Gastric Ulcer and the Use of the Stomach-tube. Flade[3] in writing on the use of the stomach-tube in gastric ulcer considers the subject from three points:

1. Are we able to make the diagnosis of gastric ulcer more certain by means of the stomach-tube?

2. Is the use of a stomach-tube in a case of suspected gastric ulcer at all justifiable or would the danger connected with such an examination be counterbalanced by a greater certainty in the diagnosis?

3. Is the use of the stomach-tube in gastric ulcer permissible as a therapeutic means?

He comes to the conclusion that the use of the stomach-tube in gastric ulcer is by no means a harmless procedure, the danger of per-

[1] Journal of American Medical Association, March 29, 1902.
[2] American Journal of the Medical Sciences, June, 1902.
[3] Münchener med. Wochenschrift, 1901, Nos. 32 and 33.

foration being especially great. He therefore maintains that the stomach-tube should not be used in a young female patient where there is suspicion of an ulcer situated in the anterior wall, and the more so, since from a diagnostic standpoint the examination of the stomach contents is of only small value. As a therapeutic measure the stomach-tube is permissible only in those cases of gastric ulcer where, during a severe hemorrhage, we wish by the local application of ice-water to stop the bleeding; otherwise it is of no value.

TREATMENT OF GASTRIC ULCER. In this condition Pariser administers bismuth in large doses (10 to 20 grammes daily), as recommended by Fleiner,[1] but does not introduce it by means of the stomach-tube. He gives the drug in water before breakfast and at night, and has the patient remain on his back three-quarters of an hour. Instead of bismuth he also uses, with the same good effect and at considerably less expense to the patient, a mixture of creta alba ℥j, talcum ℥j, and magnesia usta ℥iij to iv. Of this he gives one and a half teaspoonfuls in water. The patient must, of course, stay in bed and have a suitable diet. He does not allow the patient to get up until the ulcer has surely healed. This has taken place, according to Pariser, when the pain in the back between the tenth and twelfth dorsal vertebræ has entirely disappeared. This area of tenderness persists the longest, and may be still found even if all abdominal pain has ceased.

G. Fuetterer[2] tried experimentally to produce typical gastric ulcers in animals, and succeeded only when he injected pyrogallic acid into the circulation, thereby destroying the hæmoglobin. He concludes from his experiments that an impairment of the hæmoglobin is the *sine qua non* for the formation of ulcers of the stomach in man, and recommends the use of fresh beef juice (rich in hæmoglobin) as an essential part of the treatment of this malady. Fuetterer outlines his treatment as follows:

1. If we diagnose an ulcer of the stomach, or if, in the absence of convincing symptoms—which are so often lacking—we have cause to suspect an ulcer, we must at once ascertain the percentage of hæmoglobin.

2. We advise the patient to go to bed, either in a hospital or at home, employing the services of a trained nurse.

3. We give the juice of five pounds of beef daily, as the case may require, to bring the percentage of hæmoglobin up to the normal as soon as possible. Prepared beef extract does not give the desired result. Peptonized beef solutions are not tolerated in sufficient quantity.

[1] Deutsche med. Wochenschrift, 1902, Nos. 15 and 17.

[2] Journal of American Medical Association, January 11, 1902.

For the preparation of fresh beef juice Fuetterer gives the following directions:

1. Order five pounds of finely chopped round steak, to be brought at 8 o'clock every morning, or keep it in an ice-box from the day before. The fat should be removed before the beef is chopped.

2. Mix the meat with a teaspoonful of salt, and put it into the upper part of a double boiler. Cover without adding water.

3. Fill the lower part of the boiler with warm (not hot) water.

4. Keep the boiler on a kitchen stove for four hours, keeping the water in the lower part of the boiler just warm, so a hand can be placed on the latter without burning it. This will do, as a rule; but the use of the thermostat, regulating the temperature to 120° F., gives more uniform results.

5. Turn the beef every hour.

6. After four hours press out the juice with a potato-masher, spice, and let the patient drink it in two portions, one-half at dinner the other half at supper. Five pounds of meat will give about one pint of juice.

INDICATIONS FOR OPERATION IN GASTRIC ULCER. A. T. Cabot[1] describes the different operations now performed on the stomach, and discusses in detail the surgical treatment of gastric ulcer and its sequelæ. As soon as an ulcer has made its chronic or progressive character known and has refused to yield to rational medical treatment, then is the proper moment, according to Cabot, for surgery to step in, and by affording rest and free drainage of the stomach to favor a solid healing of the ulcer. Cabot gives the following indications for the surgical treatment of ulcer:

1. Acute hemorrhages should rarely be treated by operation; the results of interference have not been good, while the results of medical treatment have been satisfactory. When, however, a hemorrhage frequently repeats itself, even if severe in amount, it will demand operative treatment as soon as its recurrent character is plain.

2. Small, frequent hemorrhages, threatening anæmia, give a clear indication for operation.

3. Perforation of the stomach, either acute with general peritonitis, or chronic with surrounding adhesions and perigastritis, demands instant operation.

4. When an ulcer runs a chronic course, with a strong tendency to recurrence, and gradually diminishes the patient's capacity for work and for the enjoyment of life, an operation is indicated, especially when the patient is so situated as to be dependent on her daily work for support and unable to closely regulate her diet.

[1] Boston Medical and Surgical Journal, vol. cxlv., No. 9.

Perforation of the Stomach. Wiesinger[1] reports a case of perforation of the stomach with operation on the fourth day after the accident, and recovery. The case was as follows: Patient, aged thirty-six years, was troubled for the previous three and one-half years with gastric pains and vomiting. On May 15, 1902, the patient was suddenly seized with violent pains in the epigastrium, vomiting, and fainting attacks. Very soon the pains spread over the entire abdomen, and there was a stoppage of the fecal current and flatus. The patient had been treated for three days at home with opiates. His pains, however, grew more severe, and the abdomen more swollen. On the fourth day after the onset of the pain the patient was taken to the hospital in a desperate and delirious condition. Wiesinger made the diagnosis of perforative peritonitis, and immediately operated. The perforation was found in the smaller curvature of the stomach, midway between the cardia and pylorus. The operation was successful, and the patient slowly recovered.

Hour-glass Stomach. The diagnosis of this condition is illustrated by C. A. Ewald[2] in a report of two cases. The following points are suggestive for the presence of this anomaly:

1. When washing the stomach, the water which has been poured into this organ cannot be regained. (This, however, is no positive proof, as it occurs also in cases of incontinence of the pylorus.)
2. After washing the stomach perfectly clear there is a sudden return of food present. (This also may happen in other conditions.)
3. In insufflating the stomach with air, first one part of the organ bulges out, and afterward another portion becomes prominent.
4. Gastrodiaphany allows only one portion of the stomach to be illuminated. If insufflation is done afterward, and by its means shown that the air passes into another area which had not been illuminated, it is a positive proof of an hour-glass stomach.
5. Turck's bag attached to a stomach-tube and insufflated bulges out only in one portion of the stomach, while normally it extends usually over the entire gastric area.

Therapeutically, Ewald had recourse in his cases to gastro-anastomosis or to gastro-enterostomy between the dilated anterior part of the stomach and the small intestine.

Gastrocolic Fistula. Regarding the diagnosis of this condition, Labhardt[3] thinks it is easily made by the vomiting of fecal matter and partially also by the diarrhœa which sets in after the fistula is established. This latter symptom also gives a hint as to the time of occur-

[1] Deutsche med. Wochenschrift, 1902, No. 5.
[2] Deutsche Arch. f. klin. Med., 1902, p. 152.
[3] Münchener med. Wochenschrift, 1901, No. 42.

rence of the communication between stomach and colon. There are two operations to be considered in this condition, viz.: jejunostomy and colo-colostomy. The first is to be preferred, especially in patients who are run down and where the entrance of stomach contents into the colon is the principal symptom. In cases that are well nourished, where most of the gastric contents still pass along the natural route, but where there is a good deal of fecal vomiting, colo-colostomy would be indicated.

Gastric Tetany. William Gerry Morgan[1] describes two cases of gastric tetany, and details the symptoms as follows:

The attacks are usually preceded by premonitory symptoms, as a feeling of nausea, with or without vomiting; or there may be a pain or burning in the stomach, or a tingling in the finger tips, or a sense of unutterable fatigue in the group of muscles about to be affected, as occurred in his second case. At times there may be no warning of the impending attack. The spasms are almost invariably symmetrical, and usually begin in the hands and extend upward to the arms. In a few cases the spasms have begun in the toes and extended upward, involving legs, thighs, and trunk. In rare instances the attack began in the hands and extended upward until the muscles of the neck and jaws were affected.

These spasms are tonic in character, and either paroxysmal or continuous.

The prognosis in tetany, according to Morgan, depends upon the particular disease with which it is associated, and upon the nature of the attack. In a general way, in mild attacks of short duration not associated with lesions of the stomach, which are of themselves serious, a favorable prognosis may be made. On the other hand, a prolonged severe attack accompanying well-marked ischochymia is a very grave complication, and in such cases the rate of mortality is very high (70 per cent.).

The treatment of tetany should be that of the gastric disorder with which it is associated. In conjunction with it nerve sedatives, such as the bromides, should be administered.

Acute Dilatation of the Stomach. H. C. Thomson[2] describes four cases of acute dilatation of the stomach. All the patients suffered from vomiting and collapse, and did not respond to any medication; they ended fatally a few days after the onset of the disease. At the autopsy no obstruction of the pylorus was found in three of the cases, while it existed in the fourth. In the latter case acute dilatation ensued in consequence of chronic obstruction of the pylorus.

[1] Philadelphia Medical Journal, May 18, 1901. [2] Lancet, October 26, 1901.

Stiffening of the Stomach. This new phenomenon indicative of pyloric obstruction is described by J. Boas.[1] It consists of a bulging up and stiffening of the fundus of the stomach for a short while after palpating it, and resembles stiffening of the intestine found in stenosis of the bowel. I have seen this phenomenon quite often, and consider it as belonging to the picture of peristaltic restlessness of the stomach. I have also observed, and once mentioned, a case in which the dilated stomach as a whole was tetanically contracted and stiff until the stomach was washed out and emptied of its irritating material; then the relaxation at once appeared.

Exactly the same phenomenon has been described by L. Bouveret.[2] He says: "This intermittent tension of the epigastrium is a manifestation of exaggerated gastric movements. We have to deal here with a kind of tetanus of all the muscular layers of the stomach. It appears that the intermittent epigastric tension represents a steady spasm of the stomach, while the epigastric nerves represent a clonic spasm." Bouveret likewise considers this phenomenon as of great importance in pyloric obstruction.

Pylorospasmus, or cramp of the pylorus, must be often assumed in cases of gastralgia. The proof of a spasmodic contraction of the pylorus is not easily given. L. Bouveret[3] has demonstrated the existence of pylorospasmus in many of his patients, especially in women with hyperchlorhydria. When contracted it gives the impression of an oval resistance of the size of a thumb; in holding the hand over it for half a minute or so a relaxation is noticeable. Bouveret believes that what he felt was undoubtedly the contracted pylorus.

Carcinoma of the Stomach. ORIGIN FROM CHRONIC ROUND ULCER OF THE STOMACH. This is the subject of an extensive study made by G. Fuetterer.[4] He describes six cases of his own in which the cancer could be distinctly traced to a previous ulcer of the stomach. Fuetterer arrives at the following conclusions:

1. If a carcinoma develops from a chronic ulcer of the stomach, then this development occurs from those parts of the edges of the ulcer which are most exposed to mechanical irritation by the contents of the stomach.

2. In the pyloric region it is the lower pyloric margin of the ulcer which is most exposed to mechanical irritation and from which carcinoma develops. But other parts of the edges may be the ones involved when dilatations and adhesions have changed the position of the organ.

[1] Deutsche med. Wochenschrift, 1902, No. 10.
[2] Lyon Médicale, March, 1901, p. 465.
[3] Ibid., June, 1901, p. 897.
[4] Journal of American Medical Association, March 15, 1902.

3. Development of carcinoma from ulcers of the stomach in the pyloric region occurs with great frequency, while such a development occurs less often in other parts of the stomach.

4. If what has been said under our third conclusion is correct, then we must in all cases in which an ulcer of the stomach or its scar narrows the pylorus, recommend an early gastro-enterostomy, to prevent the development of carcinoma. If a gastro-enterostomy has been made, then the mechanical irritation of the ulcer in the pyloric region by food is reduced, and the severe friction necessary to produce a carcinoma will probably not occur.

5. A patient suffering from the consequences of a stenosis of the pylorus, particularly if this is caused by ulcers and scars, should, if a gastro-enterostomy is not performed, be advised to eat slowly and little at a time, and to be particularly careful about carbohydrates and especially hard crusts of bread; they should avoid crispy fried or other coarse food, and they should, as much as possible, confine themselves to liquid or semiliquid foods. A good deal of fatty food should be recommended.

6. Elderly people in particular, who have but few or no teeth and a saliva which is insufficient in quantity and quality, must be most carefully advised as to their diet, and to such cases taka-diastase should be administered.

7. From the fact that carcinoma does not develop from the large ulcers alone, but may be developed from the very smallest, the prognosis of ulcer of the stomach is bad. Our aim, therefore, should be to prevent the formation of ulcers rather than to heal them after they are found, and this may be done, at least to a certain extent, by the energetic treatment of all cases of chlorosis and secondary anæmia that come under our observation.

8. After reviewing the literature, we are now in a position to say that no one before us has laid stress on the fact that carcinoma of the stomach which develops from an ulcer originates from certain parts of their edges, and that this, while of importance in itself, will prove to be of great value when it is sufficiently considered in reference to the etiology of carcinoma in general.

Fuetterer's experimental work on animals has furnished sufficient corroborating facts, inasmuch as proliferation of the elements of the mucous membrane of the stomach occurred on edges of ulcers which had been produced by experiment. The histological qualities of such proliferations were those of an adenocarcinoma.

If Fuetterer's theory be true it is quite remarkable that but few ulcers of the stomach undergo cancerous change. On the other hand, it is well known that in most instances cancer of the stomach develops in persons not having suffered from ulcus ventriculi.

COLLOID CARCINOMA OF THE STOMACH. Burt[1] describes a case of colloid cancer of the stomach and omentum, in which the diagnosis was made during life by the microscopic examination of small pieces obtained by paracentesis. Burt could find only three other cases of colloid cancer of both the stomach and omentum reported in the literature. The condition is, therefore, a rare one. He gives a complete clinical history, with a report of the autopsy, but a description of the microscopic appearance of the tumor is lacking.

CARCINOMA OF THE STOMACH AND ELASTIC FIBRES. Meinel[2] describes a case of diffuse carcinoma of the stomach in a woman, aged seventy years, in whom the stomach was very small and contracted. Microscopically, the most interesting part was the presence of a great number of elastic fibres in the muscularis mucosæ and the muscular wall proper. Meinel found the same increase of elastic fibres and small size of the stomach in the perfectly normal organ of a woman, aged sixty-eight years. He thinks that this condition is to a certain degree physiological, in order to compensate for the loss of muscular tone in the stomach of old people, and thus prevent dilatation of the organ.

Gastric Hyperæsthesia and Its Management. The patients of whom Stockton[3] speaks presented symptoms that resembled those of hyperchlorhydria, and yet the conditions were not identical. Nevertheless the symptomatology was sufficiently alike to render it impossible to make a diagnosis without examining the gastric chemistry. There is commonly distress after eating, often occurring earlier than in hyperchlorhydria; also eructations of gas and sometimes water-brash. There is often tenderness over the epigastrium, and a sensation of vague distress after meals that leads the patient to eat sparingly; hence there is loss of flesh and strength.

The examination of the stomach contents of these cases revealed the fact that the standard of hydrochloric acid was not above the normal; indeed, it was often below that seen in active individuals in good health, and still it was apparently the hydrochloric acid and the activity of the gastric digestion that caused the distress of the patient. This was shown to be true by the relief of the patient attending the use of remedies that lessened the gastric acidity and slowed the digestion, and similar though less marked benefit, followed the selection of a diet of easily digested food.

As a diet it is best to select in the beginning one that is very bland; for instance, milk or some milk preparation. To this should be added, first, the digestible farinaceous foods, then eggs; finally, meat juice at

[1] Post-Graduate, December, 1901.
[2] Münchener med. Wochenschrift, 1902, No. 9.
[3] Journal of American Medical Association, January 11, 1902.

certain meals, and later scraped meat, meat powder, and next tender steak or chop, to which may be added some of the more easily digested vegetables. Thus the diet may be gradually increased from step to step, always being careful not to go beyond the point of toleration. When found that the allowance has been too liberal (or in case it is found necessary even with a very restricted diet), and the stomach reacts unpleasantly, it is advisable in order to relieve symptoms to give after meals antacids as soon as evidences of irritation arise. Mixtures containing sodium bicarbonate, magnesium carbonate, and the bismuth and strontium salts are commonly employed.

Enteroptosis or Splanchnoptosis. B. Robinson[1] has written an extensive paper on this subject. With regard to treatment, Robinson lays stress on drainage, abdominal supporters, and two operations, namely, gastro-enterostomy and union of the two recti abdominales in one common sheath. While the value of abdominal supporters in enteroptosis is well known and is above discussion, the other points are somewhat new and may be debated. Robinson describes drainage as follows:

"The most important treatment for splanchnoptosis from first to last is regular and ample drainage; the sovereign drainage fluid is a half normal salt solution (℥j NaCl to the quart), 8 ounces of which should be drunk every two hours for six to eight times a day. I add to each glassful of half normal salt solution one tablet, containing aloe socotrina, $NaHCO_3KH$ CO, fluid extract of cascara sagrada and $MgSO_4$, 2 grains. After four to six weeks' use the tablet is omitted, the (3 to 4 pints) half normal salt solution, with established habits, is sufficient to insure daily drainage, evacuation, and renal and cutaneous secretion. The half normal salt solution, aided by the tablet, not only drains the tractus intestinalis, the tractus urinarius, and tractus perspiratorius, but thoroughly washes the internal tissues of the body, leaving them in an aseptic condition. The patient suffers chiefly from non-drainage and from deficient and disproportionate secretion, with consequent fermentation and meteorism. Constipation is the fate of the splanchnoptotic from lack of expulsive power. Such a patient requires continual drainage, hydrotherapy. The dyspepsia frequently accompanying splanchnoptosis is mainly owing to non-drainage of stagnant contents in the digestive tract. The more the subject is drained, the less waste-laden blood with mental and physical depression, the less meteorism and intra-abdominal pressure."

It appears to me that the ingestion of these considerable quantities of water are not of much importance, and in some instances even may

[1] Philadelphia Medical Journal, December 7 and 14, 1901.

do harm. The rule is usually to rather restrict the amount of fluids in these patients with enteroptosis, as their stomachs are ordinarily in a state of atony.

The other suggestion made by Robinson, that we perform two operations on patients with enteroptosis, namely, gastro-enterostomy and union of the two recti abdominales into one sheath, appears to me not to be acceptable. Most patients with enteroptosis, if properly nourished, get along very well without an operation. The operation of gastro-enterostomy is a serious procedure, and should be done only in cases of ischochymia of a high degree after all other treatment has failed. The greater majority of patients with enteroptosis do not suffer from ischochymia at all. The second operation is likewise not essential.

Deep Inspirations as a Cure for Seasickness. Heinz[1] found, experimentally, that by producing in a dog a condition of apnœa by means of forced oxygenation he was able to inject subcutaneously $\frac{1}{6}$ of a grain of apomorphine without inducing vomiting. As soon as the apnœa stopped, retching and vomiting followed. From this he found that deep inspirations frequently repeated were of great benefit in relieving seasickness.

THE INTESTINE.

Relation of the Intra-abdominal Pressure. Aurin[2] has made a number of experiments on dogs, cats, and rabbits to determine the normal intra-abdominal pressure. For this purpose he inserted a glass canula, air-tight, into the peritoneum and connected this canula with a manometer. He found that the intra-abdominal pressure rises with quiet respiration during inspiration and sinks during expiration; with forced respiration, however, the reverse takes place. In human beings whom he tapped for fluid in the abdomen he found the same conditions to obtain.

To Check Hemorrhage by Intra-abdominal Inflation. Kelling[3] details various experiments made upon animals to check internal abdominal hemorrhage. He used a small trocar to blow air into the peritoneal cavity, and thus caused a rise of the intra-abdominal pressure, which again acted as a hæmostatic by causing an anæmia of the abdominal organs. He has never seen any bad effects, and the method has certainly been very effective in checking intra-abdominal hemorrhage in animals. He has not yet had a chance to try it on human beings. The operation itself is very simple, and the apparatus necessary to its proper performance not complicated.

[1] Münchener med. Wochenschrift, 1901, No. 38.
[2] Deutsche Arch. f. klin. Med., Band lxxi., Heft 1.
[3] Münchener med. Wochenschrift, Nos. 38 and 39.

Intestinal Putrefaction in Occlusion of Bile-duct. A. Böhm[1] carefully examined the urine for the daily amount of ethereal sulphates in cases of acute jaundice and found them considerably increased. This he considers as a proof that putrefaction in the intestine is increased when bile is absent. Bile, therefore, acts as an antifermentative.

The Action of Physostigmine and Atropine on Peristalsis. Oppenheim[2] in some experiments on rabbits regarding the treatment of meteorism found that physostigmine (or the extract of calabar bean) is a certain and powerful agent for increasing peristalsis. Small doses of atropine increase peristalsis; large doses paralyze the intestinal wall and cause tympanites and constipation.

C. von Noorden[3] reminds us of the good action of physostigmine in producing stronger peristalsis of the bowels. It is frequently given in veterinary practice to allay flatulence in horses. He, therefore, recommends it in cases of atony of the bowel in man. In common with others in this country I have been using the extract of calabar bean ($\frac{1}{3}$ of a grain twice daily), either alone or in combination with some other cathartic (podophyllin), quite extensively for the last ten to twelve years, in cases of flatulency and atony of the bowel, and I think that it can be highly recommended in this class of cases.

Pankreon in Steatorrhœa. H. Salomon[4] has made numerous experiments with regard to the action of pancreatic gland preparations in cases of intense steatorrhœa. He derived the best results from pankreon, 15 grains five times daily. In a few of his patients with distinct pancreatic disease the fat in the feces amounted to 52 per cent. of the ingested quantity. Following the administration of pankreon, however, the amount of voided fat was reduced to 19 per cent. At the same time there was great improvement in the subjective symptoms.

Treatment of Enteralgia Saturnina. Weber[5] gives some interesting histories of cases of lead-poisoning of obscure origin. In the treatment of these cases he found opium or its combination with belladonna of only the slightest value, while large doses of belladonna or of atropine ($\frac{1}{60}$ to $\frac{1}{20}$ grain) were of distinct value in influencing the pain and the constipation.

Defecation Facilitated by Pressure on Sacrum. For patients who suffer pain or bleeding during defecation Gumprecht[6] recommends the following procedure: At the moment of defecation the patient puts

[1] Deutsche Arch. f. klin. Med., 1901, p. 73.
[2] Deutsche med. Wochenschrift, 1902, No. 13.
[3] Berliner klin. Wochenschrift, 1901, No. 42.
[4] Ibid., 1902, No. 3.
[5] Münchener med. Wochenschrift, 1902, No. 17.
[6] Deutsche med. Wochenschrift, 1901, No. 43.

his flat left hand over the sacrum so that the finger tips project beyond the sacrum and coccyx. When he feels the soft parts protruding under the impulse of defecation he exerts gradually counter-pressure. The hand is not soiled in this procedure. The author claims that it materially lessens the pain and also the chance of bleeding in patients with rectal diseases.

Death following an Enema. Curtin[1] reports the case of a carpenter who for the purpose of taking an enema attached a long rubber hose with a six-inch hard-rubber nozzle to the faucet of a bath-tub. Subsequently he began to suffer from general abdominal tenderness, fever, rapid pulse, etc. A diagnosis of appendicitis was made, but no operation done, as the patient's condition did not warrant it. About twenty-four hours after taking the enema he died. At the autopsy an old ulcer that had been freshly perforated was found at the lower end of the sigmoid. Whether this perforation was caused by the nozzle itself or by the force of the water is undecided.

Dysentery. For the treatment of acute dysentery A. Plehn[2] recommends the following: As soon as dysentery is diagnosed, give two tablespoonfuls of castor oil. On the following day start with calomel tablets, ½ grain each, every hour for twelve hours; during the night the drug is discontinued. For the next two days calomel is administered in the same quantity and in the same way. During the calomel period (and for three days later) it is absolutely essential to thoroughly cleanse the mouth and gums with ratanhia tincture in water. If there is constipation another dose of castor oil is administered. After using the calomel for three days it is replaced by subnitrate of bismuth, 7½ grains, in tablets, given also every hour during the day, not at night, for a period of three days; then the bismuth is given every two hours for a few days. Plehn has been very successful with his new method of treatment, and believes its efficacy to consist in disinfecting the bowel.

Nehrkorn[3] describes the case of a man in whom a temporary colostomy for chronic dysentery was done. The patient had been suffering from severe pains and profuse bloody stools. In spite of exhaustive internal treatment he kept getting worse; the amount of hæmoglobin fell from 75 per cent. gradually to 30 per cent. The operation, which consisted in opening the colon in the left iliac region, was successful, and the patient made a good recovery.

Nehrkorn thinks that operative interference in these cases is indicated when internal treatment is unable to control the hemorrhages or the

[1] Medical Record, April 19, 1902.
[2] Deutsche med. Wochenschrift, 1901, No. 39.
[3] Ibid., No. 1.

pain, tenesmus, and profuse diarrhœa; and, secondly, when internal treatment (especially chysmata) are no longer tolerated by the body.

Intestinal Sand. Chemically, E. Deetz[1] found no cholesterin or bilirubin present; he also proved the absence of starchy material. Deetz does not believe that the sand owes its origin to some indigested cellulose matter (fruit-pits, etc.), but rather assumes that it originates from a pathological excretion of the intestine. I have seen two cases of intestinal sand myself, and found the sediment to contain microscopically organic material revealing the structure of plants (fruit-pits, hardened cellulose).

Extreme Dilatation of Colon as the result of marked constipation is reported by Geib and Jones.[2] Ordinarily the period between evacuations was about three to four months. Once the patient went without a movement of the bowels for a whole year; then it was estimated that he passed about eight gallons of feces. He died a year later. At the autopsy the colon was found very much distended, measuring 19¼ inches in circumference. The stomach and small intestines were empty.

Uncinariasis (Ankylostomiasis). The acquisition of the Philippine Islands by the United States has drawn attention to the diseases more common in the tropics. To these also belongs uncinariasis, a case of which, with autopsy, has been described by Claytor.[3] As is well known, uncinariasis is a chronic disease due to infection by a small thread-worm known as the uncinaria duodenalis (ankylostoma duodenalis), which is characterized clinically by intense anæmia, dyspnœa, weakness, gastro-intestinal disturbances, and, in advanced cases, by œdema of the face and extremities and serous effusions into the cavities of the body.

It must not be supposed that all those who are infected show symptoms of uncinariasis; far from it, as many are strong and healthy. The weak and poorly nourished are those who are least able to withstand the loss of blood occasioned by the parasite.

The worm, according to Claytor, is nearly cylindrical in shape, from 0.4 to 1 mm. ($\frac{1}{60}$ to $\frac{1}{25}$ inch) in diameter, and from 6 to 18 mm. ($\frac{1}{4}$ to $\frac{3}{4}$ inch) in length. It is yellowish or grayish-white in color, with translucent edges. The males are more slender and more transparent than the females by reason of the less extensively developed sexual organs. The head end is always bent backward. The tail, which can be distinguished by the swelling at the end (the bursa copulatrix), is much more curved than the head, sometimes appearing even to be rolled up. The length of the mature male is from 6 to 11.5 mm.

[1] Deutsche Arch. f. klin. Med., 1901, p. 365.
[2] Journal of American Medical Association, May 17, 1902.
[3] American Journal of the Medical Sciences, January, 1902, p. 28.

The ova, which are a perfect oval in shape, measure 0.055 to 0.065 mm. by 0.032 to 0.043 mm., and are covered with a transparent shell through which may be seen the segmented yolk.

The pathological anatomy is that of extreme anæmia plus the local lesions in the small intestine due to the presence of the uncinaria. There is general bloodlessness of all the tissues; œdema and effusions into the cavities; the fat is usually fairly well preserved; the heart is enlarged, dilated, and may have undergone fatty change; the spleen and kidneys are very often lardaceous and waxy, or the spleen and still more frequently the liver present a certain degree of atrophy. If the autopsy is performed a short time after death the parasites may be seen clinging by their mouths to the mucous membrane of the small intestines. If the body has grown cold they are found in the mucus.

The way to make a diagnosis of uncinariasis is first to suspect its presence. Once having had the suspicion aroused by the peculiar anxious expression of the face and the intensely anæmic appearance of the patient, it is a very simple matter to examine the stools for the ova, which are present usually in large numbers. The parasites themselves are almost never seen until after the administration of an anthelmintic.

TREATMENT. Thymol is administered as follows: 15 to 30 grains repeated four times at intervals of one and one-half to two hours. If the bowels do not act spontaneously in twelve hours after the last dose give a purgative. It is well to clear the bowels the day before with a laxative, and place the patient on liquid diet. The fact that thymol is poisonous must not be lost sight of, and the patient should be carefully watched. Since the drug is freely soluble in alcohol, ether, turpentine, chloroform, oil, glycerin, and certain alkaline solutions, these should be withheld during its administration.

In seven or eight days the stools should again be examined, and if the ova are still present the same program should be carried out and repeated until all the parasites have been destroyed.

Sprue or Psilosis. In a very exhaustive article Musgrave[1] discusses the etiology, symptomatology, and especially the anatomical findings and bacteriological aspect of sprue or psilosis as observed in Manila. It is a tropical disease, according to Manson a dangerous catarrhal inflammation, chronic in nature, affecting the mucosa of all or part of the alimentary canal, associated with suppression of or interference with the glandular functions of the organs subserving digestion. It is characterized by "irregularly alternating periods of exacerbation and quiescence; by an inflamed, bare, and eroded condition of the tongue and mucous membrane of the mouth; by flatulent dyspepsia; by pale,

[1] American Medicine, March 8 and 15, 1902.

copious, and generally loose, frothy, fermenting stools; by wasting and anæmia, and by tendency to relapse." In at least thirteen of the sixteen cases which came to autopsy, sprue existed as a state or symptom-group in other diseases; as a complication if sprue is considered a disease. The author gives several detailed clinical histories, with autopsy and bacteriological examinations, and then goes on to consider the morbid anatomy and microscopic pathology of this condition. He finally comes to the following conclusions: Sprue symptoms are nearly always found in the presence of other and well-known lesions, discoverable by careful clinical studies, aided by microscopic methods.

Careful studies of these cases by modern methods fail to indicate an additional etiological factor, and with our present knowledge it is more rational to consider sprue as a state or symptom-group (comparable to the typhoid state) occurring in the tropics in chronic diseases, especially those affecting the gastro-intestinal canal.

The following clipping from a recent editorial in the *Medical News* is quoted: "In a word, there seems to be a number of affections at present considered independent nosological entities that are really manifestations of preceding infections. The recognition of the true identity of such symptom-complexes will prove an important step in advance in our knowledge of disease, and will usually furnish valuable hints as to the therapeutics of these conditions. Possible connections of preceding infections with tissue changes that produce symptoms later are always to be borne in mind."

Acute Intestinal Obstruction. Homer Gage[1] operated successfully on a patient, aged eighty years, for acute intestinal obstruction. The symptoms consisted in pains and vomiting. The abdomen was somewhat distended, but there was no localized area of tenderness or of muscular resistance. The patient was vomiting every half-hour, and the vomitus, as well as his breath, had a very strong fecal odor. At the operation a coil of small intestine was found tightly constricted by a fatty band, which passed directly over it. The band was severed. It is of great interest to state that the same patient had undergone a radical operation for cancer of the sigmoid flexure five years previously by McBurney, and that there was no return of the growth found. Gage says:

"It was a great satisfaction to be able to examine thoroughly the contents of the abdomen, and to demonstrate the entire absence of any recurrence, so long after the primary operation for removal of intestinal cancer. In our constant battle with malignant disease such instances of long-continued immunity are most encouraging, and serve to stimulate us to greater boldness and to more radical thoroughness of excision.

[1] Boston Medical and Surgical Journal, December 19, 1901, vol. cxlv., No. 25.

"The last operation, too, emphasizes once again the value and importance of early exploration in cases of acute intestinal obstruction, even under very discouraging circumstances. To wait until the localization of the lesion is assured, or until distention has become extreme, is to wait until the chance of success is lost. At such times the operation rarely brings other than discredit upon the surgical art."

ATROPINE CONTRAINDICATED IN INTESTINAL OBSTRUCTION. Gebele[1] condemns the indiscriminate use of atropine in intestinal obstruction. He thinks that it obscures the symptoms even more than opium, and often causes death by allowing the favorable moment for operation to pass by. As an illustration he gives the history of a case that ended fatally. If internal medication is indicated in ileus, especially the paralytic form, morphine is to be preferred to atropine. With mechanical obstructions surgical interference alone is to be recommended.

The use of belladonna in these cases is not new. According to Schulz, it was first used similarly by Fuzet-Duponget in 1831, and after that especially by French physicians.

Pritchard and Aronheim report cases of ileus caused by gallstones and ileus caused by paralysis of the bowel, respectively, that were treated successfully by atropine injections.

CHRONIC ILEOCÆCAL INVAGINATION. Quadflieg[2] reports a case of long-standing ileocæcal invagination on which he operated successfully. The invaginated portion could be felt as a tumor the size of a kidney, and it was difficult to decide the nature of this tumor before opening the abdomen. In this case the abdomen was flabby, the bowels were somewhat constipated, and there was no rise of temperature at any time. There were no bloody stools and no tenesmus.

Appendicitis. The difficulty of making a diagnosis in abdominal conditions is illustrated by Brewer,[3] who presents the histories of 11 cases in which a diagnosis of appendicitis had been made, but which were shown on operation or autopsy to be due to other conditions. In 2 cases the symptoms were due to renal calculus; in 4 cases to diseases of the uterine appendages; in 1 case to sarcoma ilei; in 1 case to cholecystitis; in 1 case to acute suppurative pancreatitis; and in 2 cases to general sepsis.

These cases are exceedingly interesting, as they illustrate facts which are known to us all, but are often overlooked.

HEREDITY IN APPENDICITIS. Forchheimer[4] gives the genealogical tables of three families in order to establish the theory of the heredity

[1] Münchener med. Wochenschrift, 1901, No. 33.
[2] Ibid., No. 27.
[3] Annals of Surgery, 1902.
[4] American Medicine, 1902.

of appendicitis. Forchheimer says that by taking into consideration those factors that may predispose to appendicitis by heredity, the fact naturally obtrudes itself that there may be remote and local causes, or both together. The appendix is a rudimentary organ, and as such has less resistance to disease than one not undergoing involution. The position and direction of the appendix may also be affected by heredity.

THE DIAGNOSIS OF APPENDICITIS. Curschmann[1] has made some very interesting studies in regard to differentiating purulent from catarrhal or serous inflammations of the appendix. For this he finds that the number of leucocytes is the best index, better even than the temperature curve. He comes to the following conclusions:

1. In the great majority of cases a leucocyte count will distinguish cases of appendicitis with simple or fibrinous exudation from those accompanied by abscess, even though other signs—form, consistency of exudation, temperature, or exploratory puncture—are negative.

Non-purulent cases (light cases) show either no increase in white cells at all or only a small increase in the beginning of the disease, soon dropping permanently, or only with a few remissions, to normal. Higher leucocyte counts without abscess formation occur only in the beginning of the disease, and are then transitory. Very rarely does the count even in these cases exceed 20,000 to 22,000.

If in the first few days or, more rarely, during further observation the leucocyte count remains permanently high, provided other complications (pneumonia, etc.) can be excluded, abscess formation is certain and surgical treatment absolutely indicated.

Leucocyte counts of 25,000 or higher are alone very suspicious. If occurring after the disease has been well established, abscess formation may with certainty be predicted, and further delay of operation would be dangerous.

2. If the abscess is opened the number of leucocytes immediately drops to physiological limits. Should this not occur, retention of pus or other abscesses have to be thought of.

3. Should perityphlitic abscess rupture into the gut or bladder, etc., the same result as from surgical interference occurs, viz.: the number of leucocytes decreases, provided the pus finds free drainage.

4. In the diagnosis of abscess formation the leucocyte count stands far ahead in value of the temperature curve.

Elsberg,[2] dealing with the question "What can we diagnose in acute appendicitis?" divides his subject into three headings: 1. Can we diagnose the position of the appendix? 2. To what extent

[1] Münchener med. Wochenschrift, 1901, Nos. 48 and 49.
[2] Medical Record, April 5, 1902.

can we diagnose the changes that have occurred in and around the organ? 3. What can we determine regarding the general peritoneal cavity?

In answer to the first question, Elsberg gives an interesting new point. He found that the direction of the appendix ran, in the majority of cases, from McBurney's point to a point of greatest tenderness as pointed out by the patient himself. This method fails where there is general peritonitis or an abnormality of the colon.

Regarding the second question, the author thinks that it is generally impossible to diagnose correctly a perforation or gangrene of the appendix in a case where no mass is to be felt. In patients who give a history of acute appendicitis, and who have a mass in the right iliac fossa, we can only diagnose "acute appendicular abscess;" we can never say beforehand what pathological changes have occurred in the appendix.

In the attempt to arrive at a conclusion regarding the condition of the general peritoneal cavity, every fact of the case must be carefully weighed. Even in the absence of a rise of the pulse-rate, or a sudden extension of the pain or tenderness, Elsberg relies more and more upon marked abdominal rigidity as an indication of impending trouble in the peritoneal cavity.

Stinson[1] believes that the various phenomena of appendicitis should not be described as indicating different kinds of appendicitis, but rather as marking different stages of one kind of disease. The writer also reports a case of appendicitis in which he found two foreign bodies —two beans—which produced perforation and abscess formations. Operation was followed by recovery. From a study of the pathology of appendicitis, Stinson draws the following additional conclusions to those he has already published:

1. That as appendicitis is strictly a surgical disease, the earlier it is operated upon the better for the patient.

2. That cases operated upon early should have no mortality.

3. That during all appendicitis operations the appendix should be removed, provided irreparable damage is not done in attempting to find or remove it.

4. That where there is a local or general infection the abscess cavity or cavities should be freely opened, all adhesions separated, all pus, shreds, etc., cleaned out, all inflamed or pathological omentum excised, and all pathological intestines and infected portions of the abdomen be freely irrigated with hot water or hot saline solution until the fluid comes away clear; the intestines, etc., are then dried with sponges and returned to their normal positions.

[1] Medical Record, March 22, 1902.

5. That fecal concretions are more apt to be present as exciting causes of appendicitis than foreign bodies.

6. That foreign bodies are sometimes present in the appendix and are exciting causes of appendicitis.

7. That when the appendix contains foreign material it is more likely to be a pointed or heavy body.

8. That fecal concretions closely resemble some foreign bodies of light weight—*i. e.*, grape seeds, cherry-stones, etc.—and that when one is in doubt whether the material is a concretion or foreign body it should be carefully examined microscopically and chemically to determine the exact characters.

9. That operations such as appendectomy or somewhat similar ones —*i. e.*, those involving laparotomy—can be as readily, quickly, safely, and cheaply performed at the patient's home as elsewhere.

Evans[1] describes a case of appendicitis in a young girl, aged nine years, in whom, all the cardinal symptoms being absent, no diagnosis was made until the autopsy. The patient was sick five days. At the autopsy a straight appendix of large lumen, without foreign bodies, adhesions, or malformations, was found. There was a bacterial infection of the peritoneum, without perforation of the walls. The infection killed the patient before peritoneal symptoms had developed.

Lymphatic and Portal Infections following Appendicitis. John C. Munro[2] has described twenty cases of his own of this affection, and does not consider them rare. The symptoms are obscure, often insidious, at times fulminating. Munro believes that the degree of lymphatic infection is not dependent on the extent of the appendicial inflammation, a mild chronic appendicitis at times giving rise to a severe lymphangitis; that the lymphatic disturbance may date its origin from an appendicitis occurring many months beforehand; that persistent fever without other evident cause should suggest one or both of these infections; that spasm, tenderness, and fulness (spasm of the quadratus lumborum) indicate a retroperitoneal infection possibly due to appendicitis; that chills and hepatic tenderness, associated at times with jaundice, may be of appendicial origin, and that this origin, especially in obscure cases, should be sought for most carefully in physical examination, in the personal history, and, if necessary, in abdominal exploration; that prompt and thorough drainage of the liver, together with the removal of the inflamed appendix, offer the best means for recovery; that abdominal section, with definite free exploration of all abscesses within reach, is far more satisfactory, not more difficult, and less dangerous than aspiration.

[1] Medical Record, March 29, 1902.

[2] Therapeutic Gazette, January, 1901, and Boston Medical and Surgical Journal, January 23, 1902.

Practically all lymphatic infections are curable by operation; but if the cases are allowed to go on until they become septic skeletons before operation, the chances are almost hopeless.

In brief, a persistent temperature during or following appendicitis, inconsistent with other lesions and associated with lumbar spasm, should suggest a lymphangitis. More or less, perhaps fleeting, jaundice, irregular chills, hepatic tenderness and progressive emaciation should suggest a portal pyophlebitis following appendicitis, present or remote.

SUBPHRENIC ABSCESS FOLLOWING APPENDICITIS. In an interesting paper on subphrenic abscesses after appendicitis Elsberg[1] says that this complication is not generally recognized. He gives the literature of seventy-one such cases, and adds two of his own. He then goes on to give the frequency, anatomy, and symptomatology of the disease. Regarding diagnosis, he says: "The first symptom of importance is pain in the right hypochondrium, generally localized somewhere between the eighth and the eleventh rib, between the mammary and posterior axillary lines. Over this region there may be fine friction sounds, or dulness or flatness on percussion over the area of relative liver dulness, or over the lower ribs posteriorly. This dulness will spread beyond the area of normal liver dulness, at the same time pushing the liver downward."

If the subphrenic abscess contains gas, the liver dulness is replaced by tympanitic resonance.

Treatment is surgical, and consists in resecting parts of the ninth and tenth ribs and thoroughly draining the abscess cavity.

THE TREATMENT OF APPENDICITIS. C. Bäumler[2] publishes his clinical experience of appendicitis (perityphlitis), extending over a period of twenty-five years. He advocates the use of opiates in moderate doses, as they not only give relief to the patient, but act beneficially on the course of the disease. Bäumler does not believe that the symptoms are marred by it to any extent. Purgatives he deprecates. The application of cold poultices is recommended. With reference to operative intervention, Bäumler gives the following indications:

1. Cases in which the existence of a large abscess can be positively detected or assumed with great probability.

2. Cases in which there have been several attacks of appendicitis, with a constant tendency to recurrence.

Ochsner[3] publishes the results obtained in seventeen cases of appendicitis that were treated by rectal feeding exclusively. These cases

[1] Annals of Surgery, December, 1901.
[2] Deutsche Arch. f. klin. Med., 1902, Band lxxiii., p. 90.
[3] Münchener med. Wochenschrift, 1902, No. 8.

were all such as could not very well be operated upon at once. They usually were beyond the first thirty-six hours and had the symptoms of some complication (impending perforation, localized peritonitis, etc.). The result in all the cases was very good. The symptoms at once improved when all food by mouth was stopped, and the operation could usually be successfully performed later on.

In the treatment of acute intestinal obstruction following appendicitis, Hotchkiss[1] has derived great benefit from, first, the free use of decinormal salt solution; second, free incision into overdistended coils of gut; and, third, from the closing of the peritoneal cavity without attempting to drain it. As regards after-treatment, three measures are essential:

1. The persistent and intelligent use of the stomach-tube, with lavage.
2. The early and, if necessary, the repeated administration of saline purges.
3. The use of the rectal tube for the relief of gas, and the use of high enemata.

Stenosis of the Ileum. Groth[2] describes a case of stenosis of the ileum caused by a circular ulcer. By a process of exclusion he arrived at the conclusion that the ulcer was a catarrhal one. The patient died in spite of an enterostomy.

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Indications for Operation in Cancer of the Intestine. F. B. Lund[3] gives the following indications for surgical intervention in cancer of the intestine (without any emergencies): Operation is indicated absolutely in all cases in which a tumor is suspected of being a cancer of the intestine, after a careful eliminative diagnosis. If a benign tumor or obstruction is found so much the better.

Operation is indicated where the symptoms point to a probability of stenosis of the bowel, whether a tumor is palpable or not.

Exploratory operation is indicated whenever vague intestinal symptoms associated with loss of weight in persons past middle life lead to the suspicion of intestinal cancer. Exception should be made of cases of general metastases of the peritoneum, cancer of the liver, etc., in which event no radical operation can be proposed, but all operative measures must be directed to palliation.

With regard to the nature of the operation, that must be determined at the time in accordance with the nature of the individual case. Excision of the growth with immediate union of the ends of the bowel is the ideal to be sought. Intestinal anastomosis and enterostomy are

[1] Annals of Surgery, November, 1901.
[2] Münchener med. Wochenschrift, No. 11.
[3] Boston Medical and Surgical Journal, August 29, 1901.

merely palliative measures to be undertaken where the former is impracticable.

Tuberculosis of the Intestine. Zahn[1] finds in his statistics that primary tuberculosis of the intestine occurred in 2.27 per cent. of all cases, secondary tuberculosis occurring in 63.21 per cent. It is usually caused by the swallowing of tubercular sputum in patients who suffer from some structural changes of the stomach, viz.: chronic interstitial gastritis, glandular atrophy, cystic glandular dilatation, etc. Functional stomach troubles also may act in a similar manner, but not as frequently. He accordingly calls attention to the necessity of keeping the stomach in good condition in all tuberculous patients, and to enjoin them not to swallow the sputum.

HYPERPLASTIC TUBERCULOSIS OF THE INTESTINE. This affection seems to be quite rare. Thus far in the English literature three and in the American four cases have been described. A. J. Lartigau[2] has written a very valuable paper on the subject and reported a case of his own. At the autopsy of Lartigau's case the following condition was found in the intestine:

On section the thickened portions were resistant to the knife, and gray or whitish in color. The thickening was quite uniform in all parts of the circumference of the intestine, except in the cæcum, where it was most pronounced posteriorly; here the thickness was fully 1 cm. greater than anteriorly. To the naked eye the walls seemed to be largely fibrous. No tubercles or caseous areas were visible. The lumen was entirely patent at all points, being quite normal in the ileum except in the lower half metre, where it appeared reduced by about one-third. This narrowing of the lumen continued until the transverse colon was reached, whence the diameter gradually became more and more normal as the sigmoid was approached. The cæcum was free and the circumference of its lumen was 13.4 cm.; that of the ileum one-half metre above the ileocæcal valve was 7 cm.; that of the ascending colon 9 cm.

The most conspicuous feature of the mucosa was the presence of numerous papillomatous masses, rather clubbed in form. They were most abundant in the lower ileum, cæcum, and part of the ascending colon, where the largest attained as much as 8 mm. in length, the average size being about 4 to 5 mm. They were freely movable, but rather rigid masses of tissue, with narrow pedicles. They appeared to be covered with normal mucous membrane. In the cæcum and ileum they were most numerous and quite closely aggregated; in the remaining portions they appeared more discrete.

[1] Münchener med. Wochenschrift, 1902, No. 2.

[2] Journal of Experimental Medicine, November 29, 1901.

Many sections from different levels were stained by several methods for tubercle bacilli. These bacilli were present in enormous numbers in the epithelial layer of the lower ileum, cæcum, and ascending colon, often twenty to forty in a field (Leitz, Oc. 3, oil immersion 1/12). Higher up in the ileum and in the rest of the colon this layer contained only a few or none. The papillomatous outgrowths likewise contained only a few bacilli. In the submucosa tubercle bacilli were present in large numbers in the same regions in which they were abundant in the epithelial zone.

Although subject to considerable variations, hyperplastic tuberculosis of the intestine, according to Lartigau, presents a fairly definite pathological picture, and on the whole exhibits certain features more or less characteristic of the process. The tumor-mass may attain great proportions and bear a striking macroscopic resemblance to carcinomatous disease, but the microscopic examination reveals the true nature of the disease. The most frequent seat of the affection is the ileocæcal region; the rectum, apparently, comes next in order of frequency.

The frequency with which the lesion is localized in the cæcum and rectum is probably explicable by the fact that stasis is favored in these regions, giving opportunity for implantation of the tubercle bacilli on the mucosa.

Although the process is a remarkably slow one, progression finally leads to tumor-formation, with resulting intestinal obstruction in a large proportion of the cases; from this the patients sink gradually to the fatal issue, unless surgical intervention is invoked. In others in which no stenosis is present some terminal infection usually carries the patient off.

The *treatment* of the condition is obviously surgical; extirpation of the diseased tissue promises good results in a fair proportion of cases.

Hyperplastic Colitis. Lilienthal[1] describes a case of extirpation of the entire colon, the upper portion of the sigmoid, and four inches of the ileum, for hyperplastic colitis. At first a left inguinal colostomy was done, which improved the patient very much; then the continuity of the bowel was again restored. No sooner had this been done than her symptoms began to grow worse again; so the third operation—a right inguinal colostomy—was performed and the appendix removed. Although the patient rapidly improved, it was evident that closure of the gut would again result in a return of the symptoms. Accordingly an end-to-end ileosigmoidostomy was performed by means of Murphy's button. The colon was left in the abdomen and irrigated from the external colostomy wound. By means of a fibrous cord communication

[1] American Medicine, April, 1901.

had again become established between colon and sigmoid, and total colectomy was therefore decided upon. In spite of a pneumonia and an abscess that developed, she got along well with the exception of the fistula in the right side. This finally necessitated another operation, since which time the patient has been in good health.

THE LIVER.

Levulose for Testing the Function of the Liver. Strauss[1] thinks that we have in levulose a means of testing the function of the liver. He found that by giving levulose to patients with diseases of the liver nearly 90 per cent. had as a result an alimentary levulosuria. This occurred regularly, and was not found in absolutely healthy individuals.

Bendix and Bickel[2] think that the theory of glycolysis as advanced by Lepine and his pupils, assuming a glycolytic ferment in the pancreas, should be revised, as it does not exclude several sources of error, viz.:

1. Errors arising from the method of glucose determination.
2. Errors due to the destruction of glucose by bacteria or fermentation processes.
3. Errors arising from the destruction of glucose due to purely chemical (non-fermentative) processes.

Croftan,[3] discussing the function of the soluble ferments of the blood in intracellular digestion, says that probably each cell secretes a ferment. He draws analogies from the biology of simpler unicellular micro-organisms. He then goes on to say that it has been experimentally shown that the oxidation of fats and carbohydrates is due to the action of numerous soluble ferments that are present in the blood and lymph. These ferments are carried principally by the white blood corpuscles.

Croftan[4] has also published the results of a number of series of experiments regarding the cause of diabetes mellitus. He finds that there is a glycolytic ferment in the blood, and that this glycolytic ferment and solutions of trypsin are, if not identical, so similar that they cannot be distinguished by known methods. Until proof to the contrary is forthcoming he considers himself justified in declaring the glycolytic ferment of the blood and tissue to be none other than trypsin. A reduction of glycolysis is the principal if not the only cause of diabetes.

From these deductions the following therapeutic measures would promise some success:

[1] Deutsche med. Wochenschrift, 1901, Nos. 44 and 45.
[2] Ibid., 1902, No. 1.
[3] Journal of American Medical Association, May 3, 1902, p. 1123.
[4] American Journal of the Medical Sciences, 1902, p. 662.

1. The infusion of chyle or blood from a healthy animal.
2. The injection of leucocyte extracts.
3. The injection of trypsin.
4. The injection of vegetable glycolytic ferments.

Formation of Bile Pigment and Bile Acids. With regard to the formation of bile pigment and bile acids, A. C. Croftan[1] has made several experiments, in which he demonstrates:

1. That the bile pigments and the bile acids are not formed by the liver cells.

2. That the bile pigments and the bile acids can be formed in various parts of the organism other than the liver.

3. That the bile pigments and the bile acids can be formed from hæmoglobin outside of the organism, by a purely chemical, fermentative process, and without the intervention of the liver cells.

According to Croftan, bile pigment and bile acids are always formed whenever there is free hæmoglobin and the presence of glycogen and trypsin.

In the liver we always have a medium containing glycogen, and by conversion, dextrose; for the formation of the bile acids and the bile pigments this is the *first* condition. The *second* one is given in the presence of trypsin. The *third* is given in the constant presence of free hæmoglobin; it is derived chiefly from red blood corpuscles that perish in great numbers in the liver, "the grave of the red blood corpuscle" (Nicolaides showed that there are from one to two million less red blood corpuscles in the blood of the hepatic vein than in that of the hepatic artery); in addition, free hæmoglobin is carried to the liver in the splenic vein, that always contains some of the hæmoglobin derived from the red blood corpuscles that are destroyed in the spleen; finally, the leucocytes are known to carry fragments of red blood corpuscles to the liver, and consequently also bring hæmoglobin (Loew, Naunyn, Minkowski). In the liver, therefore, we have an intimate mixture of the three products, and consequently the formation of bile acids and bile pigment. No specific liver function is required; the rôle of the organ is that of a "mixer" of an "abdominal lung!"

If the formation of bile acids and bile pigment from hæmoglobin by the action of trypsin in the presence of dextrose is a purely chemical process, and altogether independent of the specific action of any particular group of cells, we must conclude that *wherever in the body free hæmoglobin is present, together with dextrose and trypsin, this conversion into bile products can occur;* in other words, that the formation of bile acids and bile pigment need not occur in the liver alone.

[1] Philadelphia Medical Journal, January 11 and 18, 1902.

Red blood corpuscles are constantly destroyed in different parts of the body, and consequently hæmoglobin is constantly liberated; dextrose is universally present, and trypsin in small quantities can be found in many organs, and is present in the leucocytes that can carry it everywhere. Here, then, a trinity of conditions is given for the formation of bile products in almost any part of the body.

Cirrhosis of the Liver. J. C. Wilson,[1] in a paper on this subject, draws the following conclusions:

1. The term cirrhosis is an unfortunate one. It has been applied to conditions wholly unlike etiologically, anatomically, and clinically, which have, however, in common an overgrowth of the connective tissue of the liver.

2. The term chronic interstitial hepatitis is to be preferred.

3. Alcohol is by far the most common cause of interstitial hepatitis alike in the cases in which the liver is of normal size or slightly enlarged, in the atrophic form, and in the hypertrophic form.

4. The symptoms of this condition are in many cases ill-defined, and not rarely the liver is not changed in size or contour. The clinical diagnosis in a large proportion of the cases is therefore impossible.

5. In the presence of definite symptoms and of the signs of enlargement or diminution of the liver, that is to say, in terminal conditions, the diagnosis is commonly a simple matter.

Types of Cirrhosis of the Liver. G. Ascoli[2] believes that there are two distinct types of liver cirrhosis—one, Hanot's hypertrophic cirrhosis, with icterus and usually swelling of the spleen, and Laennec's atrophic cirrhosis of the liver. In the first category the liver cells themselves are very little if at all changed, while they are atrophied in the second group. In Hanot's cirrhosis the organism is not able to retain its nitrogen balance, and there is a constant tendency to eliminate larger amounts of nitrogen than introduced by the foods. In Laennec's cirrhosis, on the other hand, there is rather a deficiency in the elimination of nitrogen, noticeably through urine and feces. Ascoli assumes that Hanot's disease consists in a toxic process involving primarily the blood and spleen, and, secondly, the liver. In Laennec's cirrhosis of the liver the disease appears to start primarily in this organ.

Cirrhosis of the Liver and Hæmatemesis. Curschmann[3] describes a case of cirrhosis of the liver in which, through collateral anastomosis between branches of the portal vein and the vena cava, fatal hemorrhage from a varix in the stomach had resulted. He gives the history of two other cases, and refers to ten more in which, as a

[1] Medical News, February 8, 1902.
[2] Deutsche Arch. f. klin. Med., 1901, p. 387.
[3] Deutsche med. Wochenschrift, 1902, No. 16.

result of cirrhosis or syphilis of the liver, fatal hemorrhage had taken place from the dilated veins of the lowest part of the œsophagus. This condition is almost always found only as a complication of chronic hepatic disease and subsequent congestion of the portal circulation.

Primary Tuberculosis of the Liver. Frank,[1] in reporting a case of primary tuberculosis of the liver, comes to the following conclusions:

1. That primary tuberculosis of the liver, though rare, may occur.

2. That the infection may take place by way of the intestine and the portal circulation, the bacilli finding entrance through an ulcer in the bowel—which in his case was, at the time of illness, of some duration—and leave no trace of the place of entrance into the body.

3. That tuberculosis of the liver may infect the other abdominal viscera and also the peritoneum secondarily.

4. That the process may cause a great increase of the connective tissue in the liver (interstitial hepatitis).

5. That the disease results fatally within twelve months.

The Echinococcus Disease in North America. I. P. Lyon[2] has written an exhaustive paper on this subject, and has collected all the cases of echinococcus disease reported in North America—241 in all. The liver is the seat of election of the parasite, being involved in almost 74 per cent. of the cases. The disease is quite rare in this country, but it appears to be on the increase. The dog and wolf represent the intermediate host of the tænia echinococcus, from which man is infected. It will be of great prophylactic importance, first, to beware of too intimate communication and handling of the above-named animals; second, to endeavor to diminish, if possible, the frequency of the disease in dogs. For the latter purpose Lyon advises that hydatid cysts found in slaughtered animals should be destroyed by burning. The practice of throwing out the offal of slaughtered animals should be interdicted by law, and dogs should be prevented from entering the premises of slaughter-houses.

Hartley[3] gives the histories and treatment of four abdominal echinococcus cysts, three of the liver and one of the peritoneum. Echinococcus cysts in the abdomen require varying operative interference, according to their situation and the condition of their walls. These various points are well brought out by the author, who also has appended to his article an extensive list of references.

[1] American Journal of the Medical Sciences, April, 1902, p. 630.
[2] Ibid., January, 1902, p. 124.
[3] Medical Record, April 26, 1902.

AFFECTIONS OF THE GALL-BLADDER.

Removal of the Gall-bladder. Lilienthal in an interesting article[1] gives the clinical histories of twelve cases of gall-bladder affections that were operated on by him. Among these cases were three in which he removed the entire gall-bladder with good success. This operation of entire removal of the gall-bladder is neither so dangerous nor so difficult in the majority of instances as one might imagine. When the diseased viscus can be safely removed it should be done, provided the gall-passages are unobstructed. In conclusion the author calls attention to the fact that, as in so many other grave abdominal diseases, the disorders of the gall-bladder and ducts respond to surgical treatment in direct proportion to the timeliness of the operation. The general practitioner should, therefore, not wait longer in gall-bladder disease before he calls the surgeon than he does in any other grave abdominal lesion.

Cholelithiasis. R. B. Preble[2] discusses the difficulty of diagnosing cholelithiasis, pointing out that tabes dorsalis, lead colic, and ulcer of the stomach sometimes simulate gallstones. With regard to treatment, Preble is not always in favor of operative intervention. The latter is indicated in the following conditions, provided the diagnosis of gallstones is positive:

1. Frequently repeated attacks of colic.
2. Septic symptoms in a patient with gallstones.
3. Empyema of the gall-bladder.
4. Localized or generalized peritonitis.
5. Persistent jaundice.
6. Obstruction of the intestines.
7. Fistulæ.

According to Brill,[3] pain is the most prominent symptom of gall-bladder disease, while jaundice is absent in 80 per cent. of the cases of gallstones. Fever is frequently observed, and when of an intermittent type and associated with jaundice it indicates, as a rule, a stone in the common duct. A careful physical examination of the patient often offers the most reliable data in forming a diagnosis of disease of the biliary passages. Sometimes, however, the diagnosis is most difficult on account of the absence both of physical signs and of definite clinical symptoms. The differential diagnosis would have to include the consideration of gastralgia, ulcer of the stomach or duodenum, intestinal colic, renal colic, malaria, peritonitis, appendicitis, ileus, hypertrophic hepatic cirrhosis, acute pancreatitis, and carcinoma of the pancreas.

[1] International Clinics, vol. iii., eleventh series.
[2] Journal of American Medical Association, April 12, 1902.
[3] Medical News, May 10, 1902, p. 876.

Boas[1] again calls attention to a sign found in connection with cholelithiasis. It consists in demonstrating an area of increased tenderness, on pressure, on the right side behind on a level with the twelfth thoracic vertebra, two to three fingers from the vertebral bodies. At a corresponding point on the left side no tenderness is found. He finds this symptom present in a majority of the patients suffering from cholelithiasis, although it may also be absent. This symptom is often present even when there is no tenderness over the gall-bladder or the free margin of the liver. In testing for this symptom he has lately modified the procedure by using the faradic current instead of the fingers for determining various degrees of sensitiveness.

Regarding gallstones and cholelithiasis, Fiedler[2] thinks that a great many more people suffer from this disease than we know of. In autopsies gallstones are found in from 5 per cent. to 10 per cent. of all deaths. He expects a good deal from the future use of the Roentgen rays. Etiologically, it is certain that typhoid fever predisposes to gallstones, and that they are formed principally from the calcium and cholesterin originating in the epithelial coating of the gall-bladder. As to operation, he believes that it is best to be conservative, and absolutely condemns the view of von Winiwarter, that as soon as the diagnosis of cholelithiasis is made an operation is indicated. He also opposes the other extreme of deferring operation until the *indicatio vitalis* makes it imperative.

Tuberculous Cholecystitis. Kisch[3] reports a case of chronic tuberculous cholecystitis. The mucous membrane of the gall-bladder seemed to have undergone cheesy degeneration and contained several gallstones and pus. Microscopically, giant cells and tubercle bacilli were found in the gall-bladder wall. The author thinks that the infection was carried by the blood.

Intestinal Obstruction Due to Gallstones. L. S. Pilcher[4] maintains that the diagnosis of gallstone as the cause of an intestinal obstruction is often obscure and uncertain. This will necessarily be the case in those not infrequent instances in which the symptoms of obstruction declare themselves suddenly and without previous signs of a cholelithiasis. Most of the symptoms that attend the condition of gallstone intestinal obstruction are at best suggestive rather than positive. The greater number of these cases occur in women over fifty years of age. The obstruction is in the small intestine, and retroperistalsis is early induced, provoking copious vomiting that soon becomes fecal, yet without the signs of shock and early collapse that mark an

[1] Münchener med. Wochenschrift, 1902, No. 15, p. 608.
[2] Ibid., 1901, No. 43.
[3] Prager med. Wochenschrift, 1902, No. 6.
[4] Medical News, February 8, 1902.

internal strangulation. For the same reason excessive tympany does not develop. The obstruction may be incomplete, and a chronicity or intermittence of the symptoms may mark the case.

As soon as the symptoms of obstruction are positive, whether the presumption of a gallstone as its cause is entertained or not, a laparotomy is justifiable, first as a diagnostic, and, secondly, as a therapeutic procedure.

Raiewski[1] describes five cases of intestinal obstruction from gallstones. The latter need not be of especially large size in order to produce ileus. They often cause irritation of the intestinal wall and subsequent contraction, thereby causing a stoppage of the fecal current. Fecal vomiting, as a rule, appears early, and the general condition of the patient is usually good. These two features are rather characteristic of gallstone ileus. With regard to treatment, Raiewski advises early operative intervention. Of course, medical treatment should be given a trial; but if it is not fully successful in a short period of time there should be no further delay, and surgery should step in.

Jaundice during Pregnancy. Two interesting cases of jaundice, occurring in two sisters during pregnancy, are described by Benedict.[2] The older sister, as soon as she became pregnant, began to suffer from general pruritus and later from jaundice. She had been pregnant four times, but always aborted in the seventh month, none of the children living.

The younger sister had the same symptoms of pruritus and icterus in her two pregnancies. The first pregnancy, however, went to full term, and the child lived and was healthy; in the second pregnancy she aborted after three months. The author thinks that these symptoms are due not so much to obstructive jaundice as to an interference with the cells and function of the liver, due to pregnancy. An analogous condition is seen in the nephritis of pregnancy.

Lavage with Nitrate of Silver Solution as a Remedy for Gall-bladder Affections. Ehrlich[3] advocates the use of lavage of the stomach with silver nitrate solution for the cure of cholangitis and cholelithiasis. He proceeds by first washing the stomach with water of 104° to 120° F. He then introduces 500 c.c. of a solution of silver nitrate (1 : 1000) of the same temperature, and allows this to stay in the stomach for one-half to two minutes. After withdrawing it he washes out the stomach with more water. Nitrate of silver by mouth works similarly, but is not quite as efficient.

[1] Deutsche med. Wochenschrift, 1902, Nos. 10, 11, and 12.
[2] Ibid., No. 16.
[3] Münchener med. Wochenschrift, 1902, No. 14.

THE PANCREAS.

Symptoms of Pancreatic Disease. Francis W. Murray[1] describes three cases of pancreatic disease. The most characteristic symptoms are fatty stools and glycosuria, and should they be found in the absence of jaundice or intestinal disease, pancreatic affection is probably the cause. According to Oser, such an origin is practically certain if, in the absence of jaundice, fatty stools, azotorrhœa, glycosuria, and a tumor in the pancreatic region are present.

Of the local symptoms of pancreatic disease, pain and the presence of a tumor are frequently mentioned as characteristic. The pain in acute affections is generally very intense, but its site is very variable. It is usually referred to the epigastrium, and it may radiate in various directions, as to either shoulder or arm, or along the left costal border to the scapula, or downward into the abdomen. As a symptom there is nothing characteristic in its site or character; it simulates exactly the pain of a perforative peritonitis or the pain of intestinal obstruction.

Concerning the etiology of pancreatic diseases in general, one finds numerous predisposing and direct causes mentioned as etiological factors, but the results of recent investigations plainly indicate that infection plays an important part in many varieties.

One case was one of pancreatic cyst, and here Murray made a positive diagnosis before the operation. There was a smooth, tense, semi-fluctuating tumor, about the size of a large cocoanut, situated a little to the left of the median line in the epigastric and umbilical regions, and extending into the left hypochondriac region. The area of flatness began just below the stomach and extended to the level of the umbilicus, where it met the resonance of the transverse colon. The patient made a complete recovery after the operation.

W. S. Thayer[2] has also written an excellent paper on this subject. In the diagnosis of acute pancreatitis the following points are, according to Thayer, of help: The patient is usually of adult life or middle age, corpulent, and, in a considerable proportion of instances, of alcoholic habits. The history of attacks of biliary colic is not infrequent. The abdomen, especially in the epigastric region, is distended, rigid, and tender; in some instances the pain may be aggravated by pressure over the lower left ribs, which is communicated directly through the spleen to the tail of the pancreas. The pain is commonly of an agonizing character, resisting even large doses of morphine, and sometimes necessitating the use of chloroform. There is vomiting of mucus, frequently

[1] American Medicine, January 25, 1902.
[2] Ibid., March 1, 1902.

bile stained. Constipation is generally present, though diarrhœa may follow. The temperature is but little if at all elevated; the pulse is usually accelerated greatly just before death. Cyanosis may be a striking symptom. In a large proportion of cases these symptoms are associated with profound prostration, and rapidly succeeded by collapse and death within three or four days.

At first the symptoms may be confounded with an attack of biliary colic, which may, indeed, as in one of his own cases, usher in the symptoms. Especially significant is the character of the pain, which is more intense and constant than that of gallstones. Its intensity, its diffuse epigastric character, with occasional localization on the left side, the profound collapse, so commonly present, should, however, suggest the true condition.

Often a diagnosis of intestinal obstruction has been made, but the epigastric localization of the pain, its peculiar intensity, the absence in the great majority of instances of stercoraceous vomiting, the sudden and profound collapse, should direct the mind of the clinician in the right direction. Especially important is the fact that in these instances the abdominal tenderness and distention are commonly localized in the epigastrium, and that distended intestinal coils and peristalsis are never observable.

The distinction from a perforative peritonitis is more difficult, but here also the suddenness and intensity of the symptoms, especially of the pain, the early collapse, and the absence of previous history of gastric or duodenal ulcer, are important points. In instances of perforation of the gall-bladder following cholecystitis the symptoms are in most instances localized in the right side. The possibility of mesenteric infarction should also be considered, and the differential diagnosis may be difficult. The position and intensity of the pain and tenderness may here be valuable points of distinction, together with the absence of those conditions commonly associated with mesenteric embolism or thrombosis (cardiac disease—arterio-sclerosis). It is rarely if ever possible to feel the inflamed pancreas, owing to the tenderness and consequent tenseness of the abdominal walls.

While this is the common picture of acute pancreatitis, yet milder attacks may occur in which a diagnosis may be difficult or impossible.

Pancreatic Hemorrhage. The diagnosis of those instances of explosive hemorrhage (pancreatic apoplexy) occurring in the absence of acute pancreatitis is based mainly upon the sudden onset of acute pain in the pancreatic region, with vomiting, followed almost immediately by collapse and death. The symptoms differ from those of acute pancreatitis only in their greater acuteness and in their more rapid course.

Chronic Pancreatitis. The commonest cause of the disease appears to be obstruction of the duct by pancreatic calculi, biliary calculi in the terminal portion of the common duct, or carcinoma of the head or body of the gland. Ascending infection may result from lesions of the bile passages or duodenum. Persistent vomiting may favor an ascending infection of the duct, with resultant sclerotic changes. Chronic interstitial pancreatitis is not infrequently associated with cirrhosis of the liver, and is apparently dependent upon the same general causes. In the pancreatitis associated with duct obstruction and ascending infection the lesion is interlobular, invading the lobules only secondarily and sparing the islands of Langerhans. Diabetes results only when the disease is far advanced. In that form of chronic pancreatitis occurring with hepatic cirrhosis, and in that observed in hæmochromatosis, the process is interacinar and invades the islands of Langerhans. With extensive disease of these structures diabetes appears to be the rule. A positive diagnosis of chronic interstitial pancreatitis is rarely possible.

Thayer arrives at the following conclusions:

Acute pancreatitis should be recognized in many instances. The importance of an early recognition of those cases which go on to extensive necrosis and to suppurative parapancreatitis is easily appreciable.

Chronic interstitial pancreatitis is to be suspected under the following conditions:

1. Instances in which glycosuria develops in an individual with chronic cholelithiasis.
2. In cases of glycosuria in association with cirrhosis of the liver.
3. In glycosuria in the course of hæmochromatosis.
4. In glycosuria following attacks suggestive of pancreatic colic.

Pancreatic lithiasis is recognizable only when calculi are found in the stools.

Cysts of the pancreas are usually to be recognized on account of their location.

Primary *cancer* of the pancreas is often latent. The presence of obstructive jaundice with distended gall-bladder and rapidly developing cachexia, in association with little or no hepatic enlargement, is suggestive of this affection.

Fatty stools—in the absence of diarrhœa or jaundice—together with indications of interference with the digestion of albuminoids, are valuable confirmatory evidence of deficiency or absence of the pancreatic secretion.

Chronic Interstitial Pancreatitis. Opie,[1] in a very interesting and exhaustive article on chronic interstitial pancreatitis, starts out by

[1] American Journal of the Medical Sciences, May, 1902, p. 845.

saying that chronic inflammation of the gland is seldom primary, but is usually associated with and the result of changes in other organs, the gastro-intestinal tract, the liver, and the bile passages. He then gives the macroscopic and microscopic appearance of two types of chronic pancreatitis, the interlobular and the interacinar form. Twenty-nine cases of chronic inflammation of the gland are reported, most of them with their anatomical findings. He classifies them according to their causative factors. Finally, he arrives at the following conclusions:

1. Chronic interstitial pancreatitis is slightly more frequent in males than in females. Two-thirds of the total number of cases occur between the ages of forty and sixty years.

2. The most frequent cause of chronic pancreatitis is obstruction of the duct of Wirsung, due to pancreatic calculi, to biliary calculi in the terminal part of the common bile-duct, or to carcinoma invading the head or body of the gland. Duct obstruction may be followed by the invasion of bacteria, which take part in the production of the resulting lesion.

3. Ascending infection of the unobstructed duct of Wirsung may follow an acute lesion of the duodenum or of the bile passages, and may cause chronic inflammation. In cases which have given a history of long, persistent vomiting, chronic diffuse pancreatitis may be found at autopsy and is probably the result of an ascending infection of the gland.

4. General or local tuberculosis is occasionally accompanied by chronic diffuse pancreatitis, affecting chiefly the interstitial tissue of the gland.

5. Chronic interstitial pancreatitis is not infrequently dependent upon the same etiological factors, notably alcohol, which produce cirrhosis of the liver; and in about one-fourth of the cases the two lesions are associated.

6. Following duct obstruction and ascending infection the lesion affects principally the interlobular tissue, only secondarily invading the lobular tissue, and sparing the islands of Langerhans. Diabetes results only when the lesion is far advanced.

7. Accompanying the so-called atrophic or Laennec's cirrhosis of the liver, the pancreas is at times the seat of a diffuse chronic inflammation, characterized by diffuse proliferation of the interacinar tissue, which invades the islands of Langerhans. A similar lesion accompanies hyaline degeneration of the islands of Langerhans and the condition known as hæmochromatosis.

8. Interacinar pancreatitis is usually accompanied by diabetes mellitus. When diabetes is absent the lesion is of such slight intensity that the islands of Langerhans are little implicated.

Sarcoma of the Pancreas. M. S. Kakels[1] reports a case of sarcoma of the tail of the pancreas, and draws the following conclusions:

The difficulties in the diagnosis of malignant pancreatic tumors are so numerous and great that we rarely find a case in the literature where a correct diagnosis has been made before operation or necropsy.

All or several of the symptoms above mentioned, together with the anamnesis, may lead to a probable diagnosis.

Recognition in the living of the nature of the growth is almost impossible.

Tumors of the pancreas are of the greatest interest to surgeons, as it has been only of recent years that operations have been made for their removal.

For surgical intervention the most important symptom is a palpable tumor.

Cysts have been incised and their contents evacuated.

Less frequently, however, have solid growths offered opportunities for surgical interference.

Removal of solid tumors with a portion of the gland itself is exceedingly dangerous and rarely successful. Even if it were possible to extirpate the gland, aside from the insurmountable difficulties on account of the bloodvessels and close proximity of the neighboring organs, the surgeon would not be justified, because, as Minkowski has shown, the entire removal of the gland is followed by rapid and fatal diabetes.

The Islands of Langerhans and Sugar. Schmidt[2] thinks that the islands of Langerhans in the pancreas bear a direct relation to the combustion of sugar. He has found that degeneration and atrophy of these tissues coincide with the presence of sugar in the urine.

Diabetes after an Old Operation on the Pancreas. Tischemacher[3] reports a case of diabetes developing eight years after an operation on the pancreas for cyst. This cyst in turn had given trouble only eight years after an injury. The case is, therefore, remarkable on account of the long time that had elapsed after injury to the pancreas before diabetes became evident.

[1] American Journal of the Medical Sciences, March, 1902.
[2] Münchener med. Wochenschrift, 1902, No. 2.
[3] Ibid., No. 16, p. 658.

ANÆSTHETICS, FRACTURES, DISLOCATIONS, AMPUTATIONS, SURGERY OF THE EXTREMITIES, AND ORTHOPEDICS.

By JOSEPH C. BLOODGOOD, M.D.

SURGICAL SHOCK.

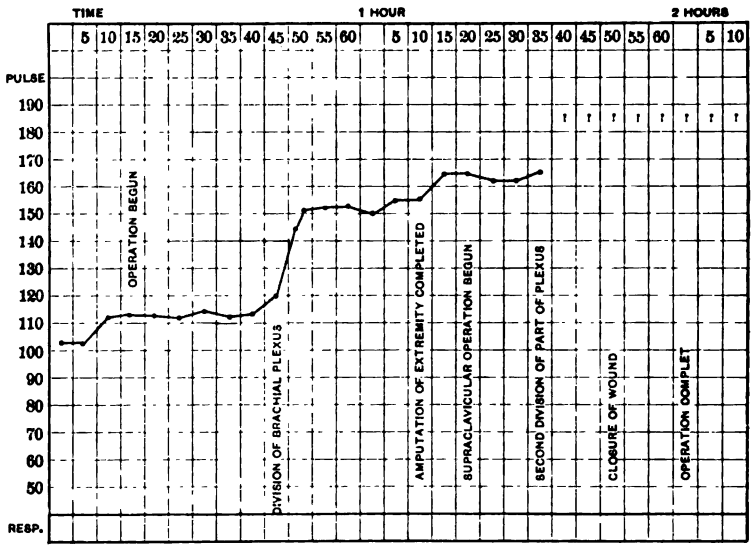
In previous numbers of Progressive Medicine (December, 1899, p. 151, and December, 1900, p. 91) I have considered fully the contributions to the literature on this most important subject in general surgery. Harvey Cushing,[1] in a recent article on "The Avoidance of Shock in Major Amputations by Cocainizations of Large Nerve Trunks Preliminary to their Division," confirms by clinical observations the experimental and clinical work of Crile.[2] In Cushing's first case, an exarticulation of the shoulder-girdle for sarcoma, profound shock with great increase of the pulse-rate followed immediately after the division of the brachial plexus. There was practically no loss of blood. As shown in his pulse-chart recorded at the operation (Fig. 3), the rate of the pulse during the first forty minutes of the operation varied between 100 and 110. Coincident with the division of the brachial plexus the pulse-rate increased in a few minutes from 110 to 150; at the end of one hour and thirty-five minutes, when there was a second division of part of the brachial plexus, the pulse-rate, which had been between 150 and 160, could not be counted. The pulse continued thready and almost imperceptible throughout the remainder of the operation, which was completed at the end of about two hours. For twenty-four hours after the operation the patient's general condition was typical of that seen in severe traumatic shock. The patient recovered, illustrating that the prognosis in this form of shock is very much better than in shock associated with or due to loss of blood.[3]

In Cushing's second case the operation was of a similar character, but in this instance, before the division of the nerves of the brachial plexus, they were cocainized; and, although there was considerable loss of blood at this operation, due to the fact that the subclavian vein was

[1] Annals of Surgery, October, 1902.
[2] Progressive Medicine, December, 1900, p. 91.
[3] Ibid., 1899, p. 151.

first ligated (loss of blood into the extremity), no shock was observed during or after the operation, nor any change in the pulse-rate. In fact, at the end of an operation of two hours and ten minutes' duration the pulse-rate was 110, while at the beginning it was about 120 to 130. At the time of the division of the cocainized brachial plexus the pulse-

FIG. 3.



rate was increased from 120 to 124, falling a few minutes later to about 105. Crile's recommendation as to the preliminary cocainization of large nerve trunks is one that should be employed on all occasions, especially in amputations for injuries associated with shock.

The Use of the Tourniquet during Amputation. Cushing believes that the application of the Esmarch bandage should be made distal to the site of amputation rather than on the proximal side, which is the more common method. This would prevent loss of blood into the extremity, which takes place to a considerable degree when for certain obstacles at the operation it is necessary to ligate the vein first, and it would prevent the flushing of the extremity after division of the nerves which is followed by vasomotor paralysis. This suggestion of Cushing differs only slightly from the method described by von Esmarch[1] in 1873. Von Esmarch first produced ischæmia by the application of a rubber elastic band to the extremity, above which the tourniquet was then applied. The elastic bandage was then removed and the amputa-

[1] Surgical Technique, American edition. New York, 1901, p. 225.

tion performed distally to the tourniquet. The first portion of von Esmarch's method has been generally given up. Senn remarks in his editorial note[1] that "very few surgeons now make an attempt to render the limb bloodless by elastic compression as a preliminary step to elastic constriction, as the limb is rendered practically bloodless by holding it for five minutes in a vertical position." In amputations for new-growths the suggestion of Cushing (von Esmarch's elastic bandage) should never be used below the tumor; its application might disseminate the disease (von Esmarch and Cushing both make this statement). Nevertheless, in high amputations for sarcoma, in which it is indicated to be as conservative as possible in regard to loss of blood, after the elevation of the limb, an Esmarch bandage can be placed in those cases in which there is room between a site above the tumor and below the plane of the proposed amputation. In operations for osteomyelitis, especially in children, I believe the method of Esmarch allows us to perform more extensive operations with less loss of blood. I agree with Cushing that in amputations we should bear in mind, and, if possible, try to prevent, especially in weak and anæmic patients, the loss of blood into the extremity. This should be done with Esmarch's elastic bandage when possible. The vein should always, if possible, be ligated first.

Amputations for Traumatic Injuries Associated with Shock. Cushing takes exception to the prevailing view that one should wait before subjecting these patients to the necessary amputation. He believes that the conditions present in the injured extremity tend to perpetuate or to increase the shock already present. This is due to the constant afferent sensory impulses caused by the irritations of the nerves in the injured limb. If a tourniquet has been applied on account of hemorrhage this increases the nerve irritation and consequently the shock. Cushing believes that the "real indication is to rid the patient of the centripetal impulses, originating in the crushed member, by cocainization and division of the large nerves, so often exposed in the mangled limb, by ligation of the vessels if necessary, and the earliest possible removal of the painful tourniquet." Attempt should be made to hold up the blood pressure by strapping the abdomen. Morphine hypodermically should be given in small amounts to relieve pain and control restlessness. Cushing advocates then an early operation, and does not consider that ether anæsthesia is contraindicated, but chloroform should never be given. This statement of Cushing is of great practical importance, and, if correct, earlier amputations might decrease the mortality.

It is not infrequent that in patients very severely shocked we

[1] Surgical Technique, American edition. New York, 1901, p. 225.

observe, after watching them a number of hours, that the condition of shock has increased. These cases are usually abandoned as unfit for operation, or when subjected to operation rarely recover. The question to be settled is whether an immediate operation would have better results. Second, in another group of traumatic cases we observe after delay an improvement in the condition of shock. In these instances the operative intervention is rarely fatal. The question to be settled here is, Would the results have been as good had we operated, as Cushing recommends, without delay? These questions can only be settled by future clinical observations. Surgeons should familiarize themselves with the recent work on the physiology of shock. While the physiological questions are by no means settled, nevertheless, we know from experimental observations the chief cause of shock is due to the loss of vasomotor tone. Practically in the treatment of shock it is most important, first, to prevent further loss of blood, to replace lost blood by a non-irritating salt solution, and to prevent further vasomotor weakness by such rational treatment as will lessen or inhibit afferent sensory impulses. We can prevent or inhibit these depressing sensory impulses by keeping the patient absolutely quiet, by avoiding all manipulations which give rise to sensory impulses, by small doses of morphine, by cocainization if possible of the nerve trunks to block these impulses, and by removal of the cause of nerve irritation as quickly as possible. Vasomotor tone is best maintained by the elevation of the patient, head down, by bandaging the limbs, and, most important, by strapping the abdomen. The patient should be kept warm by external heat. Subcutaneous and intravenous infusion increase arterial tension. It is a question whether the usually employed hypodermics of strychnine, atropine, nitroglycerin, whiskey, and ether are of any value; in fact, they may be harmful. Theoretically, it does not seem rational to stimulate the vasomotor centre in the medulla already almost paralyzed by the numerous and continuous afferent impulses due to the traumatism. These patients, therefore, in the condition of shock should have the immediate benefit of this more rational treatment; the Esmarch bandage should be removed, if possible. If the Esmarch bandage cannot be dispensed with I agree with Cushing that the operation should not be delayed. If there is little or no hemorrhage, and an Esmarch bandage is not necessary, the question of immediate operation is not yet settled. I cannot quite agree with Cushing that the question of delay in traumatic shock can be answered in the same manner as in the treatment of shock from intestinal perforation. In the latter there is no doubt that no improvement can be expected by delay; but in the former the tremendous experience of practical surgeons cannot yet be thrown aside, that in many cases of

traumatic shock distinct improvement follows the delay under appropriate treatment, and that these patients' chances are increased by this delay if any extensive operative interference is demanded. But there may be, and undoubtedly are, cases in which this delay acts against rather than for recovery. These cases we may be able to select by a more careful study. Nor can I agree with Cushing entirely that ether anæsthesia is not contraindicated in extreme conditions of shock. He agrees with this himself in operations for intestinal perforation, advocating local cocaine anæsthesia. In traumatic shock we frequently must produce ether anæsthesia; but I feel that experience demonstrates that the anæsthetic time should be as short as possible, and I believe further experience will demonstrate that the results will be better if the operation can be performed without pain under the infiltration and intraneural cocaine anæsthesia.

THE TREATMENT OF HEMORRHAGE.

Steam. Prof. Sneguireff,[1] of Moscow, reports on his experiments and clinical experience with water steam as an hæmostatic. He finds experimentally that steam is a safe and reliable method of checking parenchymatous hemorrhage from organs like the liver, spleen, and kidney. He reports a case with great detail where he used steam in a partial resection of the spleen. The steam is applied to the bleeding surface through a tube or after it passes through a perforated metallic box. The latter is the best method, as it reduces the force of the escaping steam and increases the area of contact. He finds that steam not only checks hemorrhage from the tissues (parenchymatous hemorrhage), but even from vessels of fair size. During its application the surrounding tissues should be protected from the steam by gauze previously cooled in cold salt solution.

Air. Kelling[2] has demonstrated in experiments on animals that air introduced into the peritoneal cavity under a pressure of 50 mm. checks intraperitoneal hemorrhage even from vessels of considerable size.

Suprarenal Extract. This drug is considered to act both locally and generally as a hæmostatic. However, there is little in recent literature favorable to its use. It is not mentioned by von Esmarch and Bryant,[3] in their recent works on operative surgery, in the treatment of hemorrhage. Kenworthy[4] records excellent results after the internal administration in fourteen cases of hæmoptysis. Applied locally I

[1] Archiv f. klin. Chirurgie, 1902, Band lii. p. 547.
[2] Münchener med. Wochenschrift, 1901, Nos. 38 and 39.
[3] Loc. cit., p. 224.
[4] Medical Record, 1901, vol. lix. p. 415.

have observed one case of distinct toxæmia. A short time after a second application to the wound of about 5 to 10 grains of the powder the patient became suddenly very pale and the pulse very rapid. The powder was immediately removed from the wound by irrigation, but the tachycardia and extreme weakness lasted for almost twenty-four hours.

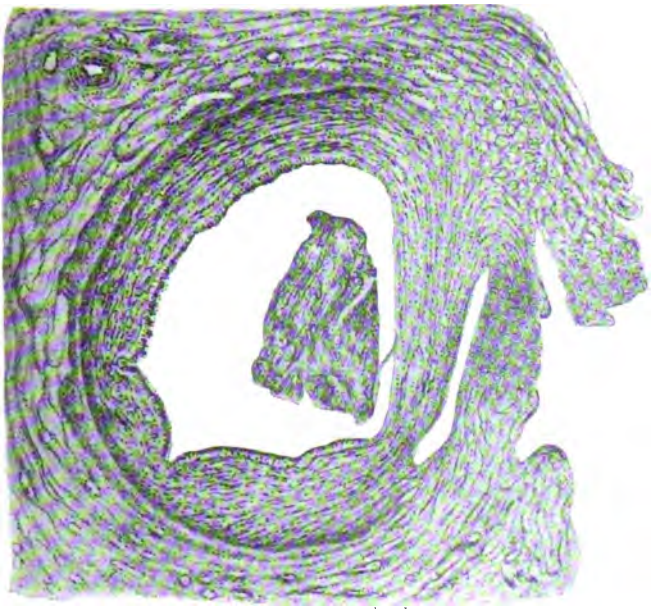
Electrothermic Pressure. Andrew J. Downes,[1] of Philadelphia, illustrates his electrothermic angiotribe and the necessary electrical paraphernalia for its use. Downes recommends it for clamping the broad ligament in various operations on the uterus and tubes, for removal of the appendix, and for the operation for hemorrhoids. This method of checking hemorrhage does away with the use of the ligature.

Ligation of Arteries. Now and then, in cases of severe hemorrhage from inaccessible points, quite radical operations must be instituted sufficiently early to save the life of the patient. Keen[2] reports two cases of ligation of the external carotid, one for hemorrhage after tonsillotomy, and one for hemorrhage following a slight intranasal operation. In both of these cases the usual local means failed. After the ligation of the carotid hemorrhage ceased at once. Frommer,[3] from the surgical clinic of Trzebicky, in Krakow, Austria, reports in detail eight very interesting cases of secondary hemorrhage from the open wounds after incision in the treatment of extensive phlegmons of the extremities. To check this hemorrhage it was necessary to ligate the larger artery. This report is of special interest to me because I have seldom observed such an extensive secondary hemorrhage in similar infections; yet this possibility must be borne in mind, and the excellent results here, after the ligation of the artery, will indicate at once the proper treatment if the usual means of checking the hemorrhage fail. The paper is of additional interest because Frommer has demonstrated from a histological study that the hemorrhage was due to the extension of the inflammation to the walls of one of the larger arteries, with the resultant necrosis and weakening of the wall. Figs. 5 and 6 illustrate the perforating ulcer in the wall of the popliteal artery, and Fig. 4 the microscopic section of the same, showing the total destruction of the wall of the artery at one point, from which the hemorrhage took place. This patient (Frommer's Case 7) was a man, aged thirty-four years. He was admitted to the hospital seven days after an injury near the left knee. The injury consisted of an incised wound from an ax, which was followed quickly by infection. On admission the limb above and below the knee was the seat of an extensive phlegmon.

[1] Journal of American Medical Association, July 12, 1902, vol. xxxix. p. 75.
[2] Annals of Surgery, 1901, vol. xxxiv. p. 21.
[3] Archiv f. klin. Chirurgie, 1902, Band lxvii. p. 439.

The treatment consisted in free incisions and the opening of the joint. At the end of the week it was necessary to make further incisions in the thigh. Ten days later there was extensive hemorrhage from the open wound in the popliteal space, which was controlled by packing.

FIG. 4.



Four days later a second hemorrhage, which was fatal. Although evidently indicated, the femoral artery was not ligated. The eighth case reported by Frommer was similar to Case 7, just mentioned.

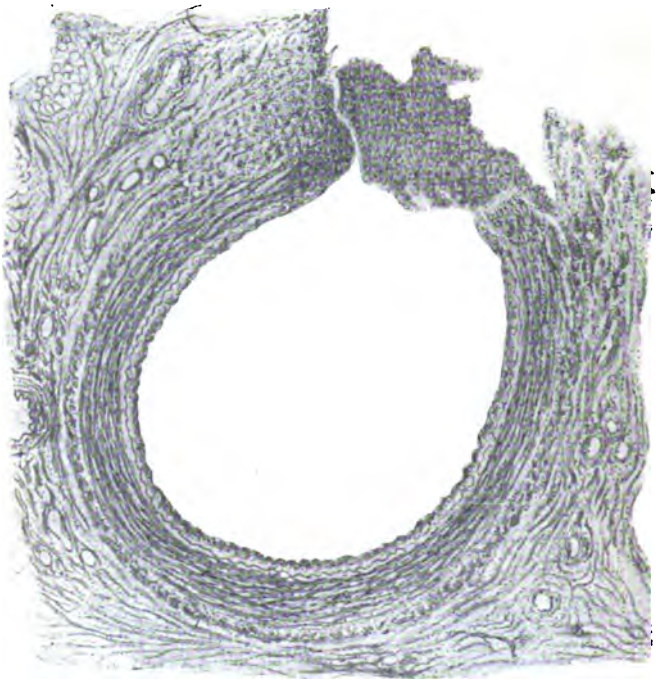
FIG. 5.

FIG. 6.

The secondary hemorrhage from the open wound in the popliteal space took place in the second month. The femoral artery was ligated in Hunter's canal, checking the hemorrhage. The patient died later from the infection. The examination of the popliteal artery showed a con-

dition similar to the one illustrated in Case 7. The other six cases recovered. Case 1, a phlegmon of the hand and forearm, ligation of the brachial artery above the elbow-joint on the twelfth day for hemorrhage. Case 2, also a phlegmon of the forearm; in this instance the hemorrhage from the ulnar artery was checked by ligation of the ulnar artery above the point of the necrosis of the vessel; previous pressure had failed to control the hemorrhage. Case 3 was similar to Case 1; the ligation of the brachial artery checked the hemorrhage at once, while tamponing on previous day failed. In Case 4 the radial artery was ligated; in Case 5 the posterior tibial artery, and in Case 6

FIG. 7.



the ulnar artery. We observe that five of the six successful cases were situated in the upper extremity; in two the brachial artery was ligated, in two the ulnar, in one the radial artery; in the sixth case the phlegmon was of the foot and lower leg, and the hemorrhage from the posterior tibial artery. The two fatal cases were very extensive phlegmons of the entire lower extremity, and the point of hemorrhage from the popliteal artery; one patient died of hemorrhage, but here the artery above was not ligated; in the second patient the femoral artery was ligated and the hemorrhage checked; but the patient, weakened undoubtedly by the loss of blood, died from infection.

In every case an examination demonstrated that the bleeding point was from the artery, the walls of which were the seat of necrosis secondary to the inflammation. The histological study of the sections of the artery confirmed the naked-eye appearances. Fig. 7 is a section of the brachial artery showing an earlier stage of necrosis than that shown in Fig. 4.

Calcium Chloride. Zibell claims that the therapeutic effect of the gelatin solution is due to the calcium oxide. The chloride of calcium has frequently been used to increase the coagulability of the blood. According to Dawson,[1] a solution containing even as much as 0.026 per cent. of this salt is dangerous as a subcutaneous or intravenous infusion. For this reason it should not be used in combination with gelatin or salt solution. It can, however, be given by the mouth. It should be tried in cases of hæmophilia in addition to other treatment. Wallis[2] records good results with calcium chloride as a prophylactic against hemorrhage in cases of hæmophilia in which it was necessary to remove teeth or do some minor operation. It is given in small doses two or three times a day for a week. In view of the danger of secondary hemorrhage after operations on patients who have been deeply jaundiced for a number of months, I believe that they should be given the benefit of the doubt by this calcium chloride treatment. Apparently the only disagreeable effect is constipation.

Salt Solution Infusions. The therapeutic value and methods of saline infusion have been previously fully considered.[3] I find nothing in recent literature to add to the indications, contraindications, or methods discussed at that time. Apparently the most important as yet unsettled question is with regard to the best solution for subcutaneous and especially for intravenous infusion. Tavel,[4] in 1892, and recently, advocated the addition of 0.25 per cent. sodium carbonate (washing soda) to a 0.75 per cent. salt solution. This solution, he claimed, increased the alkalinity of the blood, and, therefore, its bactericidal power. For this reason Tavel recommends this solution for subcutaneous infusions in all cases of infection. Küttner,[5] writing from von Bruns' clinic in Tübingen, warns us against the use of Tavel's solution. He observed six cases of extensive gangrene of the skin, with one death, after the subcutaneous use of Tavel's solution, while in many more observations with the subcutaneous injections of the physiological salt solution no complications whatever followed. In studying the

[1] PROGRESSIVE MEDICINE, December, 1900, p. 113.
[2] La Semaine Méd., 1902, No. 20.
[3] PROGRESSIVE MEDICINE, December, 1900, p. 107.
[4] Revue de Chirurgie, 1902, vol. xxvi. p. 278.
[5] Beiträge z. klin. Chirurgie, 1902, Band xxxv. p. 272.

question experimentally he found that the irritation, in some instances leading to gangrene, was due without doubt to the sodium carbonate. This fortunate observation of Küttner is enough to contraindicate the use of this salt in saline solutions. According to Küttner, we have as yet no solution which gives better results than the physiological salt solution (0.6 per cent. sodium chloride). Laufer[1] in his critical review discussed all the saline solutions recommended by the various authorities. According to von Koranyi,[2] a sodium chloride solution of about 0.91 per cent. is designated as isotonic with the blood in the majority of instances. We know that the isotonicity of the blood varies, but we have no method of determining it for the case in question. Laufer was not willing to commit himself in recommending any specific solution, but the consensus of opinion seems to favor a sodium chloride solution from 0.6 per cent. to 0.9 per cent. strength. Cushing[3] recommends a modification of Ringer's solution, using von Koranyi's recommendation as to the strength of the sodium chloride. The solution is as follows:

Sodium chloride (NaCl)	0.9
Calcium chloride (CaCl)	0.026
Potassium chloride (KCl)	0.01
Distilled water (H_2O)	99.064

In view of Dawson's[4] very careful experimental physiological work and his conclusion that Ringer's solution containing as much as 0.026 per cent. calcium chloride is dangerous, the amount of this salt, if used at all, should be reduced to at most 0.01 per cent.

When introduced subcutaneously the composition of the saline solution is very much less important than when introduced intravenously, and it seems as if the physiological question as to the best solution for intravenous solution is not yet settled. What we wish is a non-toxic solution isotonic with the blood.

In view of the excellent results of subcutaneous infusion, one should not employ the intravenous method except in those cases in which it is distinctly imperative.

[1] PROGRESSIVE MEDICINE, December, 1900, p. 107.
[2] Zeitschrift f. klin. Med., Band xxxviii., Heft 1 and 2.
[3] System of Physiological Therapeutics (Cohen), vol. lx. Philadelphia, 1902.
[4] Loc. cit.

GELATIN.

Tetanus following Subcutaneous Injection of Gelatin. Bass,[1] in his collective review of the literature up to March, 1900, reports no cases of tetanus following gelatin injections, nor are any recorded in the more recent articles of Sackur,[2] Sailer,[3] and Zibell.[4]

Recently five cases of fatal tetanus following gelatin injections subcutaneously have been reported by Kuhn,[5] Gerulanos,[6] Georgi,[7] and Lorenz[8] (two cases). Noticing these cases of tetanus infection, Levy and Bruns, of Strasburg, investigated the question whether the ordinary gelatin used contained the tetanus bacillus, and whether our usual mode of sterilization was sufficient to destroy without a doubt the tetanus spores. In their first report[9] they made preliminary notice of the presence of tetanus in many samples of gelatin. In their second and more complete report[10] they record the presence of the tetanus bacillus and its spores in eight out of thirteen samples; and their investigations on the method of sterilizing gelatin solutions demonstrate that the usual one of boiling the solutions in a water-bath is insufficient to destroy the tetanus spores. It requires at least forty minutes at a uniform temperature of 100° C. to destroy all the tetanus spores, and this can be accomplished only by placing the glass flask containing the gelatin solution (the flask plugged with cotton) in an autoclave for at least forty minutes.

These cases of tetanus infection and the investigations of Levy and Bruns should impress us with the importance of the most careful and complete sterilization of the gelatin solution, which can be easily accomplished in the ordinary steam autoclave. In cases of emergency in which we are not quite certain of this more perfect sterilization it would be safer to give the patients a prophylactic injection of the antitetanus serum.

Schmiedicke[11] also reports on the presence of tetanus bacilli in commercial gelatin.

[1] Progressive Medicine, December, 1900, p. 103.
[2] Mittheilungen aus den Grenzgebieten der Medicin und Chirurgie, 1901, Band. viii. p. 188.
[3] Therapeutic Gazette, August 15, 1901, p. 508.
[4] Münchener med. Wochenschrift, 1901, No. 42.
[5] Ibid., 1901, No. 48.
[6] Deutsche Zeitschrift f. Chirurgie, 1901, Band lxi. p. 427.
[7] Ibid., p. 439.
[8] Ibid., p. 584.
[9] Deutsche med. Wochenschrift, 1902, No. 8.
[10] Mittheilungen aus den Grenzgebieten der Medicin und Chirurgie, 1902, Band x. p. 235.
[11] Deutsche med. Wochenschrift, 1902, No. 11.

The Hæmostatic Use of Gelatin. The critical reviews of Bass and Nichols,[1] and the more recent article by Joseph Sailer,[2] of Philadelphia, were favorable to the use of gelatin.

On the other hand, Sackur[3] is less favorable to the use of gelatin, and in addition finds distinct dangers. Sackur could not confirm the results of Dastro and Floresco that gelatin increases the coagulability of blood. He used both acid and neutralized solutions. Under the microscope he found that if one drop of blood was added to one drop of gelatin there was an immediate and marked agglutination of the red blood cells. This agglutinating effect of gelatin on the blood, Sackur thinks, explains the vessel thrombosis with areas of hemorrhage in the lungs and kidneys found at the autopsies on his experimental animals. Sackur concludes as follows:

"As the admixture of gelatin to the blood can undoubtedly cause a coagulating process in the living organism, it must be conceded that under especially favorable circumstances the coagulation furthering effect may be used for hæmostatic purposes where other measures fail. Such favorable circumstances are presented by all sac-shaped spaces filled with blood. A paradigm for this are the so-called bleeder-joints in hæmophilia. In this affection, in view of the hopelessness of any other therapy, one would have to try to deposit the gelatin solution directly in the joint cavity filled with blood. There is already one communication, by Krause,[4] according to which, in a youthful bleeder with threatening recurrent joint effusions, the gelatin therapy (injections into the joints and subcutaneous tissues) was introduced with good result.

"The subcutaneous injections may further be effective in a hemorrhage of the lungs when it owes its origin to an aneurism in a lung cavity; in one word, present prospects of success where the place of hemorrhage answers the requirement of Lancereaux—'slackened circulation and altered vessel walls.' But in the application of gelatin subcutaneously one should always bear in mind the danger which threatens the patient from formation of coagula at other places of the vascular system than that of the hemorrhage. It follows that we may only use the subcutaneous injection of gelatin in such patients in whom the irresistible hemorrhage threatens to bring about the death of the patient. The eventuality of a thrombosis will then have to be taken as the lesser of two evils."

Zibell[5] claims that his experiments demonstrate that the coagulable effect of the gelatin solutions on the blood is due to the presence of

[1] PROGRESSIVE MEDICINE, December, 1900, p. 103.
[2] Loc. cit.
[3] Loc. cit.
[4] Münchener med. Wochenschrift, 1899, No. 47.
[5] Loc. cit.

calcium oxide (lime). This is present in the usual gelatin solution in about 0.6 per cent. Zibell agrees with Sackur that thrombosis may take place not only in the bleeding vessels, but in other parts. The original investigators, Carnot, Dastre and Floresco, Lancereaux and Paulesco,[1] attribute the hæmostatic effect to gelatin. Camus and Gley[2] from their experiments concluded that the effect was due to the acidity of the solution, and that in neutralized gelatin solution the coagulability of the blood was not increased. On the other hand, Boignet, Klemperer, and others demonstrated that neutralized solutions were as effective as acid solutions. Tovölgyi[3] was unable to demonstrate that gelatin solutions increase the coagulability of the blood. The experimental results, therefore, leave us somewhat in doubt.

Clinically there seems to be evidence that gelatin does increase the coagulability of the blood, and in those in whom we have no other means of checking the hemorrhage subcutaneous injections of gelatin are justifiable.

Gelatin in the Treatment of Aneurisms. The collective review of Sorgo,[4] in 1899, made two years after the introduction of the method by Lancereaux and Paulesco, was not favorable to the subcutaneous injection of gelatin except in certain cases. In a second report Sorgo[5] found that there were good results only in sacular aneurisms, and he was unable to conclude whether this result was due to the action of gelatin or to the rest and diet. He agrees with Sackur that as yet we have no experimental proof of the coagulating action of gelatin administered subcutaneously. He, however, believes that the injections, provided asepsis is carefully preserved, are devoid of danger.

Grenet and Piquard,[6] in their careful study of 100 cases of aneurism collected from the literature, conclude that we have nothing positive, and that the entire subject of subcutaneous injections of gelatin must be reconsidered both clinically and experimentally.

From this we must conclude that one should be quite certain that the aneurism is a sacculated one before the gelatin treatment is begun. It should be combined with absolute rest in bed and restricted diet; the injections may be repeated twenty-five or thirty times.

It is interesting to note that gelatin was used locally as a hæmostatic in the third century by the Chinese. Y. Miwa[7] calls attention to this and to its later introduction into Japan. He finds an interesting

[1] Progressive Medicine, December, 1900.
[2] Arch. de Physiologie, 1897.
[3] Ungarische med. Presse, 1899, No. 30.
[4] Centralblatt f. die Grenzgebieten der Medicin und Chirurgie, 1899, Band ii. p. 10.
[5] Zeitschrift f. klin. Med., 1901, vol. xlii., Parts I. and II.
[6] Arch. Gén. de Méd., 1901, 78, Ann. N. S. v., 641.
[7] Centralblatt f. Chirurgie, 1902, Band xxix. p. 249.

account of its use in the famous book *San-Han-Ron*, a work on pathology and therapy, by the Chinese physician Chain Chiyun Kiyun, written about A. D. 200.

ANÆSTHESIA.

The Choice of the Anæsthetic: Ether or Chloroform? The great difference of opinion as to which is the better anæsthetic to be used in the majority of operations has previously been discussed.[1] It is an extremely important question to settle, because in the vast majority of operations the individual to be subjected to anæsthesia exhibits no special contraindications to either anæsthetic, but the conscientious surgeon is anxious to choose the anæsthetic which is less dangerous. Poncet's[2] contribution on 29,000 personal anæsthetizations, with only one immediate death—a child with organic heart disease—is the best that has appeared during the year. It is quite natural that he should be emphatically in favor of ether as the routine anæsthetic. He prefers ether alone rather than any of its mixtures. He agrees with Gerulanos[3] that it has not been proven that the post-operative pulmonary complications are more common after ether than after chloroform, but takes the view to which the majority of other authorities are now inclining, that the majority of post-operative pneumoniæ are of infectious etiology, and should not be called anæsthetic pneumoniæ.

On the other hand, Crouch and Corner[4] studied 3000 anæsthesiæ given during twelve months at St. Thomas' Hospital in London. They observed 10 post-operative respiratory complications, all of which followed ether narcoses. It is important to note that 7 of these took place during the hot months of the year; 1 of these patients died. During the same time there were 600 chloroform narcoses, with no respiratory complications. These gentlemen estimate the death-rate from chloroform as 1:3000, and their post-operative respiratory ether deaths as 1:2400. From this they conclude that chloroform should be considered the anæsthetic of choice. I do not think that any observation extending over only twelve months is of sufficient value to allow positive conclusions. The writers of this paper are not familiar with the literature on post-operative pneumonia, and their single death from bronchopneumonia may have been infectious in origin and probably would have occurred if chloroform had been the anæsthetic.

The Immediate Mortality of the General Anæsthetic. During the past year in Baltimore I have had (by personal communication) the

[1] PROGRESSIVE MEDICINE, December, 1901, p. 116.
[2] Gaz. Hebdom. de Méd. et de Chir., March 6, 1902.
[3] PROGRESSIVE MEDICINE, December, 1901, p. 126.
[4] Lancet, May 24, 1902.

report of one case of sudden death during a perfectly uncomplicated Cæsarean section. The patient was young and apparently in good health; the operation was performed early in labor, because of a contracted pelvis. The death occurred without apparent warning after delivery of the child during the suture of the uterus. This question is settled, that the occurrence of sudden death during uncomplicated operations takes place with the rarest exceptions and only under chloroform anæsthesia.

I also have to record (from personal communication) one sudden death under ether narcosis. This, however, can be explained by the complication—extreme anæmia. The patient, a child suffering with chronic osteomyelitis of the femur, showed a hæmoglobin percentage of 40. This is another observation to warn us of the dangers of anæsthesia in extreme anæmia.[1] The death in such instances cannot be attributed to any special anæsthetic.

Depage,[2] in reporting two cases of chloroform death during the operation, informs us that an attempt at resuscitation was made by immediately exposing the heart by free incision and giving it massage. In both cases the method failed. In one it had absolutely no effect; in the other a slight effect, but only temporary. Depage also mentions two other cases in which electrolysis of the heart was used. In one case the patient was kept alive for three hours, in the other it was successful. Anything is justifiable in these cases of sudden collapse under chloroform during the anæsthesia, but in the majority of instances it is futile.

Late Deaths after Chloroform. Cohn[3] records a late death from chloroform from Sonnenberg's clinic in Berlin. The patient was an apparently healthy girl; the operation a simple laparotomy for the removal of adherent tubes. Careful examination of the patient's urine before the operation was negative. The narcosis was an uncomplicated one, except the patient required more than the usual amount of the anæsthetic. After operation convalescence was uninterrupted until the second day. Jaundice was then noted, and the urine contained albumin and epithelial casts. There was no fever. The patient died on the fifth day in coma. The autopsy showed the characteristic lesions of chloroform death, fatty degeneration of the organs, and the catarrhal nephritis which Fraenkel[4] considers specific of the chloroform toxin. From this observation and the consideration of the numerous literature Cohn is inclined to change his views on chloroform and advises that perhaps it should not be used as a routine anæsthetic. There seems no

[1] PROGRESSIVE MEDICINE, December, 1900, p. 100, and December, 1901, 207.
[2] Centralblatt f. Chirurgie, 1902, Band xxix. p. 17.
[3] Deutsche Zeitschrift f. Chirurgie, 1902, Band lxiv. p. 189.
[4] Virchow's Archiv, Band cxxvii. p. 381, and Band cxxix. p. 254.

question that there is a protracted effect of chloroform, which in a certain number of individuals is fatal. The chloroform remains a number of days, and perhaps longer, in the body. Kast and Mester[1] have demonstrated in the urine after chloroform narcosis a combination of chloroform and some organic substance which reduces Fehling's solution, and no doubt explains many of the so-called cases of post-operative glycosuria. Büdinger[2] has demonstrated chloroform in the expired air up to five days after the narcosis. He believes that it was retained by the mucus in the nasopharynx, and this explains some of the bad late effects. He recommends careful cleansing of the naso-pharyngeal and the oral cavities.

If further observation demonstrates that the post-operative respiratory complications are as common after chloroform as after ether narcosis, the question as to the choice between ether and chloroform as the routine anæsthetic will be settled in favor of ether. Chloroform will, therefore, only be used in those cases in which our experience has demonstrated that ether is contraindicated.[3]

Blood Pressure during Ether and Chloroform Narcosis. Blauel[4] has contributed a most extensive and valuable article on this subject. It is of chief importance because it was one of the first to record the blood pressure during a large number of ether and chloroform narcoses. The conclusions demonstrate positively that when other factors are eliminated the arterial tension during an ether narcosis is well maintained and usually slightly increased, while in chloroform narcosis there were observed great fluctuations and, as a rule, a lower blood pressure. Important practical conclusions can be made. Chloroform should never be given in shock or in any cases in which a lowering of the vasomotor tone would be dangerous to the patient. On the other hand, chloroform would probably be the better anæsthetic if not contra-indicated by other factors in cases of arterial sclerosis in which there might be danger of apoplexy from the increased arterial tension of ether. This work of Blauel is another factor to be used against chloroform as a routine anæsthetic.

Nitrous Oxide and Ether. Norris[5] gives us a very interesting comparative study between 150 cases anæsthetized with nitrous oxide gas followed by ether and 150 cases with plain ether narcosis, from the gynecological clinic of Dr. Clark. The facts may be summarized as follows:

[1] Deutsche Zeitschrift f. klin. Medicin, Band xviii., Heft 5 and 6, p. 8.
[2] Centralblatt f. Chirurgie, 1902, Band xxix. p. 71.
[3] PROGRESSIVE MEDICINE, December, 1901.
[4] Beiträge zur klin. Chirurgie, 1901, Band xxx. p. 271.
[5] University of Pennsylvania Medical Bulletin, 1902, vol. xv. p. 178.

	Nitrous oxide and ether.	Ether.
Time to anæsthetize	3⅓ minutes.	13.5 minutes.
Amount to anæsthetize	60 grammes.	101.5 grammes.
Total amount of anæsthetic	170.5 "	218.0 "
Duration of administration	1 hour.	1 hour.
Pulse-rate	90 to 105.	105 to 115.

This comparison demonstrates that with the preliminary anæsthesia by nitrous oxide gas the anæsthetic time for complete narcosis is reduced by about ten minutes, and the total amount of ether by about 40 grammes. The pulse is slower; the respiration, however, is slightly more rapid. Norris also thinks that there is less shock, and post-operative nausea and vomiting are less frequent. This observation is an additional proof of that already recorded in the literature,[1] that nitrous oxide gas has taken an important place among general anæsthetics. We need, however, observations of larger numbers of cases and also observations of the blood pressure during the administration of nitrous oxide gas.

Local Anæsthesia. The technique of local anæsthesia is well established, and we can expect very little from further study. It is a form of anæsthesia that has wide application, but unfortunately is as yet not as generally employed as it should be by the general profession. I believe it should be recognized that an operation possible under local anæsthesia is unjustifiable under general anæsthesia. In reports of cases in which the operation was performed under spinal anæsthesia one is surprised to find simple operations like that for hydrocele subjected to this new and more dangerous procedure. No operation which can be performed under local anæsthesia should be attempted with spinal anæsthesia. The subject of local anæsthesia has been fully discussed in a previous article.[2]

Spinal Anæsthesia. Last year, after going over the literature on this subject very carefully,[3] I came to the conclusion that spinal anæsthesia was in its experimental stage, and that it was unfit as yet for general employment. Bier, who introduced the method, came to the same conclusion, and warned the profession against its indiscriminate use. During the last year we find less in the literature on spinal anæsthesia, and I find nothing to demonstrate that as yet the method can be recommended for general employment. Reclus[4] finds six to eight deaths among 2000 cases of spinal anæsthesia, and advises the profession to be guarded in its use. Dandois[5] reports a case of paraplegia with incontinence of urine and feces, beginning on the eighth day, fol-

[1] PROGRESSIVE MEDICINE, December, 1901, p. 135.
[2] Ibid., December, 1901, p. 140.
[3] Ibid., December, 1901, p. 150.
[4] Centralblatt f. Chirurgie, 1902, Band xxix. p. 6.
[5] Ibid., p. 19.

lowed by insomnia and delirium. The patient fortunately recovered after a month's illness. Julliard[1] records a death from apoplexy twenty-four hours after spinal anæsthesia. The autopsy demonstrated a ruptured artery in the Sylvian fissure. This was a very unfortunate result, because the patient was suffering with a simple hydrocele which could have been cured under local anæsthesia. Trzebicky[2] reports 138 cases of spinal anæsthesia. In only 103 cases was it successful. From his experience he comes to the same conclusion as Bier, that the method should only be attempted in selected cases, in well-arranged surgical clinics, with the hope of such improvement that it may take the place among safe methods of anæsthesia. Kallionzis,[3] like Tuffier, is enthusiastic, and will not admit that a single post-operative death can be attributed to the spinal anæsthesia as the direct cause. Tsakona,[4] after an experience with 120 cases, with a complete success in each case, very naturally advocates its more general employment.

OPERATIVE TECHNIQUE.

The general practitioner wishing to inform himself on the latest improvements in operative technique and the details of the various operations in surgery will find two recent books of value—one by Bryant,[5] of New York; the second by von Esmarch, of Kiel, the American translation edited by Senn.[6] I shall refer to these books in the discussion of the recent literature.

Hand Disinfection. One is surprised to find that von Esmarch[7] has very little to say on this subject. He recommends Fürbringer's method, which consists, in addition to the careful scrubbing with green soap and very hot water, with brushing of the hands for one minute with 80 per cent. of alcohol and the short immersion in an antiseptic solution (1:1000 bichloride). Gloves are not mentioned. In the disinfection of the skin of the patient von Esmarch[8] insists upon the importance of a full bath; for operations on the extremities and pelvis a soaking in specially constructed tubs (foot tub, arm tub, and pelvis tub). The remainder of the disinfection is done on the operating-table. He does not mention whether before or after anæsthesia. The operative field is first shaved, the skin is then rubbed with ether or spirits of turpentine, and scrubbed, first with soap and water, and then with a

[1] Centralblatt f. Chirurgie, 1902, Band xxix. p. 71.
[2] Ibid., p. 72.
[3] Revue de Chir., 1901, No. 10.
[4] Gazette de Gynec., April 15, 1902.
[5] Operative Surgery: D. Appleton & Co., New York, 2 vols.
[6] The Macmillan Company, New York.
[7] Loc. cit., p. 4.
[8] Loc. cit., p. 14.

1 : 1000 sublimate solution. The last scrubbing of the field of operation is done with iodoform ether.

Bryant,[1] on the other hand, recommends a more energetic disinfection, and advocates the use of rubber gloves, or, if not the glove, at least the rubber finger-stalls. He mentions three methods: First, the usual scrubbing, then alcohol and a long immersion in a hot antiseptic solution; second, the method which has been employed in the Johns Hopkins Hospital since 1889. In this method, after a thorough scrubbing with green soap and water, the hands (forearms in some cases) are immersed in a saturated solution of permanganate of potash, then in a hot saturated solution of oxalic acid until the permanganate is entirely discolored. The excess of these solutions is washed off with a sterile salt or 1 : 1000 bichloride solution. The hands and forearms are then soaked for five or ten minutes in a 1 : 1000 bichloride solution. The last method discussed by Bryant is called the nascent chlorine method, introduced by Weir. Here the surgeon takes about a tablespoonful of bleaching powder (the ordinary commercial chloride of lime) and about a cubic inch of common washing soda (carbonate of soda); to this he adds enough water to make a thin paste in the hollow of his hands; with this the hands and forearms are scrubbed as one would scrub them with green soap. During this procedure chlorine gas is given up. This scrubbing should be kept up for about five minutes. The hands and forearms are then rinsed in sterile water. In describing the preparation of the skin of the field of operation Bryant uses but a few lines. After the usual scrubbing with soap and water the skin is rinsed with alcohol, chlorine water, or a strong solution of carbolic acid; then the part is wrapped in wet antiseptic towels until the operation begins.

In view of the fact that the disinfection of the skin is the most difficult and the most important part of the technique of every operation, much more space should be given this subject in all works on operative technique, and the most improved methods should be described with the greatest detail.

It is unfortunately quite true that the best way for one to learn the details of operative technique and the various surgical operations is at the operating-table in some large surgical clinic. Nevertheless, many practitioners who must do a certain amount of surgery wish to keep themselves informed on the best method of technique, and must have some reference book to look up the details of various surgical operations. Excellent as these two works just mentioned are in the majority of their chapters, the part on the disinfection of the skin and the surroundings of the field of operation in all its details is disappointing.

[1] Loc. cit., p. 100.

Recent Literature on Hand Disinfection. I cannot agree, nor does recent literature agree, with the statement of Ochsner,[1] that "theoretically strong chemical disinfectants are indicated for the purpose of disinfecting the hands. Practically, careful washing with the mildest, viz.: soap and water and alcohol, is absolutely sufficient and very much safer for the patient, because hands roughened by the use of the strong antiseptics are much more likely to become hopelessly septic than hands which are covered with smooth, healthy skin."

The recorded experiences of all large operative clinics and all experimental work is in favor of a combination of mechanical and chemical disinfection of the hands and field of operation. It, however, is quite true, as Ochsner says, that hands roughened by the use of strong antiseptics are more dangerous than smooth hands kept clean by a simpler method of disinfection. However, I am quite certain that it is possible to disinfect the hands and the skin with a combination of mechanical and chemical disinfection, and keep them just as smooth, free from all cracks and irritation, as with the simpler methods. This has been my experience during ten years with the method followed in Dr. Halsted's surgical clinic. Nevertheless, every surgeon's skin is not so immune to the almost daily disinfection with antiseptics. For this reason hand disinfection is not only a general, but a personal question. I wish, however, to impress the general practitioner with the fact that all experimental work and clinical experience are emphatically in favor of some form of chemical disinfection of the skin, and the use by the surgeon and his assistants of gloves.

The voluminous laboratory experiments demonstrate that no method of disinfection can produce absolute sterility of the skin; that is, bacteria are always to be demonstrated in the deeper layers of the skin and in the sweat glands. Chemical disinfection, however, reduces the number and the virulence of the organisms, so that in the vast majority of instances the bacteria introduced into the wound from the hands of the surgeon or skin of the patient are insufficient in numbers and degree of virulence to produce any reaction. This laboratory result has the most important practical significance. We should always consider the hands and the skin of the operative field to be more or less infected.

The surgeon and the general practitioner should constantly avoid contact with virulent infections. In every operation for an infection the surgeon should wear gloves; if possible, infected patients should be examined with gloves; infected wounds, if they must be handled, should be handled with gloves. In the majority of instances the entire dressing can be done with instruments. With this care one avoids

[1] Chicago Medical Recorder, February, 1900.

infecting his hands and later rubbing these bacteria of great virulence deep into the hair and sweat follicles. Every practitioner frequently must see on the same day a patient suffering with the most virulent infection and an obstetrical patient. No method of disinfection will remove the streptococci from his hands, and the possibility of fatally infecting his parturient patient is fearfully increased. Yet how often this must take place, and unnecessarily so. The keeping of the hands from contact with virulent infections is the first requirement in any method of hand disinfection. Fortunately, it is true that virulent bacteria do not live long in the skin or its glands, perhaps only a few days. Nevertheless, we should conscientiously follow this first rule as far as possible. Second, all injury and irritation of the skin of the hand, and especially about the nails, should be avoided, and when present promptly treated, because in these even slight abrasions the most virulent bacteria can live, and it is practically impossible to disinfect. Thirdly, the mechanical scrubbing of the skin is the most important. It should be prolonged (five to ten minutes); the hottest water possible should be used.

Mohaupt[1] has demonstrated that sweating aids greatly in eliminating the bacteria from the hair follicles and sweat glands; and as scrubbing of the skin only removes the superficial germs, we must continue it for some time in hot water, in which the hands perspire, and thus remove more and more of the deeper bacteria. The mechanical disinfection is the most important in removing all scales and dirt from the superficial layers of the skin, and with it the germs contained therein. We must remember that after this thorough mechanical disinfection there are still some germs on the surface and many more in the deeper layers of the skin. The chemical disinfection, although very important, chiefly disinfects only the superficial layers of the skin; it removes some bacteria, and by its germicidal action greatly inhibits the virulence of the remaining germs. We must also remember that during the operation, especially if there is much sweating of the skin, germs are constantly coming to the surface of the skin from its deeper layers. For this reason the old rule—never true, but, unfortunately, so constantly followed—that the hands once disinfected remain so during the entire operation if they are not brought in contact with any non-septic material, should be discarded. When the hands and arms are not protected by gloves and a sterile-sleeved gown, they should be frequently immersed during the operation in an antiseptic solution. The more the sweating the more frequently this should be done. The skin about the field of operation should be protected as closely as possible

[1] Deutsche Zeitschrift f. klin. Chirurgie, 1901, Band lviii. p. 141.

by wet towels, quite frequently changed. One should avoid as much as possible touching, and especially rubbing, the skin of the patient with instruments, sponges, or ligatures; yet how frequently one sees a sponge swab the skin near the field of operation and then go into the wound. The irrigation of the wound, if it is necessary, should be most carefully performed. How often one sees the skin surrounding the wound washed, using the wound as a receptacle. When surgeons do not wear gloves the wound should not be handled. The majority of operations can be done with instruments without touching or entering the wound with the fingers or hand. Halsted has always practised and taught this. König[1] has recently come out most emphatically in favor of this method. If one must handle the wound, gloves should be worn.

A Substitute for Bichloride of Mercury. A number of surgeons find the constant disinfection with a sublimate solution produces a very inconvenient irritation and frequently eczema, and for this reason must give up its use. Carbolic acid solutions cannot be used to any extent without irritation. For this reason surgery is in need of a substitute for bichloride—one that will be equal in its disinfecting powers, but without its irritating effects. Blumberg[2] reports on his experimental work in the laboratory of Rubner, and the practical results in the clinic of Mikulicz in Breslau. He states that his own and the experimental work of the majority of others all point to the importance of chemical disinfection, and that the purely mechanical methods have given in Germany not only bad experimental but bad clinical results.

Blumberg has worked with a new combination of mercury (*mercury ethyl endiamin*). The first drug used was a combination with a citrate of mercury; but this had an objection, as it could not be manufactured in solid form. Later the chemists were able to make a salt with the sulphate of mercury. In a very extensive experimental investigation Blumer compared these two ethyl endiamin compounds of mercury with the usual sublimate solutions. They were found to be equal to the sublimate in germicidal power in solutions of equal strength; even much stronger solutions than those necessary to use in ordinary disinfection produced no irritation. This solution of mercury is much more stable than sublimate, and for this reason penetrates more deeply into the skin. The sulphate can now be made in tablets for convenient use, and this tablet is much more quickly soluble than the ordinary bichloride tablets. If this work of Blumberg is confirmed it will be a very important addition to skin disinfection. This mercury sulphate, ethyl

[1] Centralblatt f. Chirurgie, 1900, Band xxvii. p. 905.
[2] Archiv f. klin. Chirurgie, 1901, Band lxiv. p. 746.

endiamin, has been placed on the market under the name of "sublamin," and can be purchased in this country. I should advise surgeons who find the ordinary solutions irritating to try this new drug.

Operating Gloves. We must not expect that the covering of the hands with an aseptic glove entirely prevents the possibility of hand contact infection. Every operator who has had a long experience without and with the use of gloves reports emphatically on the better results in healing and the decrease in the even before rare instances of virulent operative infections. To demonstrate this one must have careful records of the course of the healing of the wound in a number of cases extending over a considerable period of time. These records show emphatically a great decrease, almost an elimination of the early acute infections of the wound, a marked decrease in the late infections, especially the late stitch abscesses from buried ligatures. In 1898[1] I found that the introduction of rubber gloves had reduced the suppuration of wounds after operations for hernia from 9.6 per cent. to 1.7 per cent.; from 1899 to the present time the percentage of suppuration in the wound varies from 1 to 2. While previous to the introduction of gloves, from June, 1898, up to December, 1896, we had had 11 cases of acute infection within thirty-six hours after operation, since the routine wearing of gloves by both operator and assistants from this date up to the present time we observed no acute early infections. If properly employed there seems no question that the danger of hand infection is much less when gloves are worn. Nevertheless, it cannot be denied that excellent results are obtained with the ungloved hand properly disinfected. McBurney[2] condemns the use of the naked hand in operations, and considers thin, well-fitting india-rubber gloves absolutely essential to the practice of aseptic surgery.

The latest experimental work on the question of operating gloves is by Heile,[3] from Mikulicz's clinic and Flügge's laboratory, in Breslau. Heile finds that beneath the rubber glove the hand sweats, and that very quickly there is a great increase in the bacteria on the surface of the skin. The uninjured rubber glove does not allow these bacteria to pass through; but if the glove is injured in any way the danger of infection is greatly increased. This is a very important fact to bear in mind in using rubber gloves. They should be changed, boiled again, and the hands redisinfected, always between operations, and now and then during long operations. Now and then during an operation a surgeon may wish to examine the wound without the glove. In this

[1] Johns Hopkins Hospital Reports, vol. vii.
[2] New York Medical Journal, March 22, 1902.
[3] Beiträge zur klin. Chirurgie, 1902, Band xxxii. p. 725.

instance it is a much better technique after removing the glove to re-disinfect the hand before palpating the wound. Torn rubber gloves are dangerous. This experimental work demonstrates that the hand should be just as carefully disinfected when one proposes to operate with gloves as without. The thickest glove that can be worn with convenience is much safer than a thin glove, as naturally the latter is more liable to injury. The very thin rubber gloves which seem to be most popular in this country should be condemned. The thicker glove is more expensive, but my own experience teaches that, on account of its durability, it is the most economical glove in the end.

Thread Gloves. According to Heile, these allow a certain number of bacteria to penetrate, the thicker thread glove much less than the thin. There is much less sweating under the thread glove than under the rubber glove, and for this reason less elimination of bacteria from the deeper layers of the skin. In addition, the thread glove absorbs the large majority of the bacteria eliminated, and there is no accumulation between the glove and the skin, as observed with rubber gloves. The filtration of bacteria through the cotton glove is increased when the glove is wet, and especially when it is wet with blood. Dry, thick thread gloves have, therefore, certain advantages over rubber gloves: they are cheaper; if changed frequently, especially when they become saturated with blood or fluid, they are probably as safe as a thick rubber glove, and there is no accumulation of bacteria on the surface of the hands, and no sweating. For this reason, the removal of the glove, or a tear in the glove, exposes a less infected hand than under a rubber glove. Until this work of Heile I opposed the use of cotton gloves, but I believe this work demonstrates their usefulness and safety. Surgeons who do not wish to incur the expense of thick rubber gloves, or who find that they cannot manipulate as well with thick rubber gloves, or whose hands perspire and become irritated under rubber gloves, will undoubtedly find the thread gloves a good substitute. The glove should be sterilized dry, and should be changed quite frequently during the operation. I have had no practical experience with thread gloves, and as yet can see no good reason for giving up the thick rubber glove, which I have used since 1896.

Chirol as a Substitute for Rubber Gloves. Kossmann,[1] of Berlin, introduced this in 1900. After the usual disinfection of the hands they should be dipped in alcohol and ether and then allowed to dry in the air. The dry hand is then immersed for ten seconds in the solution of chirol. This immersion gives the hand a thin, uniform coating, which dries in about three minutes. Kossmann claims that this coating does not allow

[1] Centralblatt f. Chirurgie, 1900, Band xxvii. p. 585.

any penetration of bacteria, and that there is no sweating or accumulation of bacteria on the surface of the skin. The coating is smooth and firm, it does not scale, and is not removed during the ordinary friction of an operation. Hands so protected can be disinfected in strong bichloride solutions and even in 5 per cent. formalin solution without injury to the thin veneering. He claims that there is absolutely no impairment of touch under chirol. For this reason it has many advantages over gloves. Schäffer[1] does not confirm Kossmann's work, and claims that his experiments demonstrated that germs penetrated, that it comes off in scales, and that the hands sweat under it. If Kossmann's work is confirmed, or if a substitute without any objections is found, this method of coating the hands may find a distinct place in operative technique. It will be economical, it will save time; the impairment of touch under gloves is a distinct disadvantage in certain operations, and here a protective coating without this disadvantage would be welcomed by operators. It would be a very rapid and convenient form of protection in obstetrical examinations and examinations of the rectum, and in performing autopsies on infected cases. Most pathologists find gloves very inconvenient.

Air Infection. With Lister and during the early years of antiseptic surgery air infection was considered paramount; then the pendulum swung to contact infection, and air infection was practically regarded as eliminated. Now that we have improved our methods to such a degree of excellence that the dangers of contact infections are greatly reduced, the possibility of air infection is again being investigated. Von Esmarch[2] speaks of the danger of dust. As a rule, the bacteria settle with the dust, but the commotion during an operation will again distribute bacteria in the circulating air. For this reason von Esmarch advocates the most careful disinfection of the operating-room previous to the operation. The dust should be removed with moist cloths, and in instances after infected cases the room should be disinfected with formalin gas. Heile[3] has made a number of interesting experiments. He finds that in the air of the large amphitheatre during the days on which this room is not used, and the air therefore is quiet, the average number of germs to a plate is 5. Just before the clinic, when the dust is stirred only by the attendants preparing for the operation, the number of colonies is increased to 45. After the entrance of visitors and students there is an increase to 155, which gradually drops to 14 three hours after the clinic is over. In the small aseptic operating-room, during the days on which there is no operation and no commo-

[1] Centralblatt f. Chirurgie, 1901, Band xxviii. p. 89.
[2] Loc. cit., p. 3.
[3] Loc. cit.

tion, the number of colonies per plate varies from 1 to 3. During an operation with the ordinary small number of visitors and attendants the number of colonies increases to 60, decreasing again slowly after the commotion has ceased. He has also demonstrated that the increase in the number of germs is not due entirely to the distribution in the air of the germs already present in the room; but parallel experiments show that visitors to the room increase the number of colonies, this increase being in fair proportion to the number of visitors. These experiments prove the danger of dust in the operating-room and the increasing number of germs distributed to the circulating air by visitors. Fortunately the character of the ordinary germs in the dust and those carried to the operating-room on the visitor's clothes are in the majority of instances not pathogenic; and although the great number of colonies on the plate conclusively demonstrate that the wound must also be contaminated, yet such contamination of the wound is relatively harmless. But if virulent bacteria are in the dust of the room, or are carried to it by visitors, these experiments prove the possibility of their distribution in the air and the final entrance of a certain number in the open wound. Heile's second series of experiments demonstrated the possibility of such a distribution of virulent bacteria to the surrounding air. He confined his work to cases in the hospital wards—one of pyocyaneus infection, one of streptococcus, and one of staphylococcus pyogenes aureus. He dressed these patients with sterilized instruments, gloves, and a sterile gown. Before the dressing the surrounding air and the surface of his gown was free from these bacteria. After the dressing, from the air and on his sterile gown he was able to demonstrate the presence of these pyogenic germs to a considerable extent. This demonstrates that during the dressing of infected cases we can distribute to the surrounding air, the dust, and our clothes the virulent bacteria present in the wound. For this reason the ward and the clothes of the dressers become contaminated. Dressing or operating on infected cases in the operating-room produce the same contamination. This distribution of virulent germs from infected cases is greatly decreased by moist dressings, to which the germs cling. It is the dry dressing that gives up the bacteria quickly to the air and to contact.

Such excellent experimental work has practical significance. Infected cases should be isolated, if possible; the dressing should be moist and not allowed to dry; the dresser should not come to the operating-room without changing clothes. A sterile gown, with sleeves, put on in the operating-room, should be worn by the surgeon and all the assistants.

Visitors who come near the field of operation should wear smooth, clean gowns. We should give extra attention to the cleanliness of

the operating-room. Infected dressings should not be allowed to dry in this room, but immediately be placed in some antiseptic solution. Dry dust should never be allowed to accumulate; the room should be cleaned with moist rather than dry cloths a few hours previous to the operation; commotion should be avoided as much as possible before and during the operation; there should be special care of the large amphitheatre. We must be especially vigilant when operating upon large, open wounds which are exposed to the air for a considerable time. The possibility, although rare, of a distribution of virulent bacteria in the circulating air, and their contamination of the large, open wounds, should be borne in mind and precautions taken.

Nöggerath's[1] experiments confirm Heile's. Nöggerath also studied the pathogenicity of the ordinary germs in the air, and, fortunately, finds that in the majority of instances they are non-pathogenic, and even the pathogenic bacteria soon lose their virulence in the air or dust. For this reason they are more easily destroyed in the wound, the danger of general infection is less, and the local reaction is delayed and of less severity.

FRACTURES.

Fractures and dislocations cannot be properly taught nor understood without illustrations showing the visible external deformity, the X-ray shadow of the normal, and that of the injured part in question, together with the anatomical preparation illustrating clearly the relation of the fracture to the surrounding soft parts, and the method of dressing. Such complete illustrations are as necessary here as with anatomy. These requirements for illustration we find in the excellent *Atlas of Fractures and Dislocations*, by Helferich, of Greifswald.

Especially the general practitioner, and even the more experienced surgeon, will find such a reference book of great value in the diagnosis and treatment of fractures.

The Diagnosis of Fractures. Although we must admit that the introduction of the Roentgen ray has simplified the diagnosis of fracture, nevertheless, previous to this surgeons were able in the majority of instances to make a pretty accurate diagnosis. It would certainly be a depreciation of the art of surgery to allow the use of the X-ray to prevent or lessen our ambition to make a correct diagnosis of a fracture without its aid. The relation of the X-ray to the clinical diagnosis of a fracture should be the same as that of the clinical and naked-eye diagnosis to the microscopic in surgical pathology. The latter, the

[1] Deutsche Zeitschrift f. Chirurgie, 1901, Band lviii. p. 277.

X-ray and the microscope, should be used to improve and confirm the former. This scientific use of the X-ray and the microscope has the most practical value, because our clinical and naked-eye diagnosis are improved, and one's ability to make a diagnosis without the aid of the X-ray or the microscope is greatly increased. This is of especial importance because in many instances the use of the X-ray or the microscope is inconvenient or impossible.

When possible, the X-ray should be used in every case of fracture—first, to confirm the diagnosis; second, to demonstrate the proper reduction. In the majority of instances, except in hospital practice, it is inconvenient to use the X-ray at the first dressing of the fracture. Here we make the diagnosis, reduce and dress the fracture, and later employ the X-ray to demonstrate that the fragments are in good position. In fractures of the lower extremity in patients treated at their homes, a portable X-ray apparatus may be used. I would urgently advise every practitioner to have this X-ray examination made, if possible, not only for the benefit of the patient and his own satisfaction, but for protection in suits for malpractice. In any community in which there is a portable X-ray apparatus, I feel quite certain that the physician who has a case of fracture should resort to this modern method of aiding diagnosis.

It must also be remembered that there are some fractures in which the diagnosis can be made with any certainty only by the X-ray. For this reason an X-ray examination should be made in every doubtful case in every community in which there is an X-ray machine. The practical objection to the X-ray in fractures is the expense. This objection assumes large proportions in the smaller communities, where there are few physicians whose practice is scattered over a considerable area, but it can be overcome in the majority of instances by the combination of a number of physicians in purchasing a portable machine. Even a small charge will amply pay the interest on the principal involved. Nevertheless, as far as I know, this is seldom done in this country.

The majority of surgical cases can be transported to the nearest expert, but fractures must be treated by the general practitioner, and if his results are to be compared to that of the expert he should at least be provided with the same armamentarium. Although the surgeon can relieve the general practitioner of the responsibility of most of the surgery which demands expert treatment, fractures cannot be eliminated from general practice in small communities. For this reason, the diagnosis and treatment of fractures should be given a much more important place in the curriculum of the department of surgery in our medical schools.

The Treatment of Fractures. In this country I believe that we are slow in adopting simpler and more rational methods in the treatment of fractures in general. The influence of the older methods is still paramount, that is, prolonged fixation and infrequent dressings. Absolute immobilization in the treatment of fractures is unnecessary; it delays union, because it interferes with the proper circulation necessary for the formation of bone tissue. Too firm dressings produce anæmia of the muscles, which is always followed by atrophy and sometimes, especially when the pressure is great, by an ischæmic, interstitial, fibrous myositis, from which the muscles do not recover. Years ago Billroth called attention to the fact that in fractures of the jaw and the clavicle in which absolute immobilization of the fragments was impossible, and in which there was always slight motion between the fragments, bony union was always more rapid than in fractures of other bones of equal diameters. The experience of men of unquestionable authority demonstrated that slight motion at the seat of fracture, provided the fragments remain in correct position, aids the rapidity and solidity of osseous union. Next to the perfect approximation of the fragments good circulation is of importance to insure rapid and solid union. Therefore, in the treatment of a fracture, reduction and the proper approximation of the fragments is of first importance. Every recent authority emphasizes and reiterates this so frequently neglected point in treatment. Anæsthesia is usually necessary for proper reduction, and an X-ray examination to confirm the same. After the reduction a simple dressing should be applied which will retain the fragments in proper position. This dressing should be of splints or plaster-of-Paris with or without extension and counterextension, or extension alone according to the position of the fracture. Whatever the dressing, it should be well padded and applied with as little constriction as possible. The dressing should be frequently changed to allow the bathing and massage of the extremity. If possible, the patient should be allowed to walk early in the treatment of fracture; in fractures of the upper extremity in practically every case after the first few days; in fractures of the lower extremity, with certain exceptions to be discussed later, after the first or second week, in some form of ambulatory dressing.

Massage and Passive Motion in the Treatment of Fractures. There is only one objection to massage and passive motion of the joints in the neighborhood of fractures, and that is the danger of producing displacement of the fragments. This danger varies with the situation of the fractures. Woolsey,[1] of New York, gives us an excellent résumé

[1] Annals of Surgery, vol. xxxii., 1900, p. 351.

of the subject, and states that in his experience of some four years he has demonstrated to his own satisfaction that his results are very much better when combined with proper massage and passive motion, although he does not go as far as Lucas Championnière, who recommends discarding splints very early in the treatment. All recent text-books, Helferich, Scudder, and Stimson agree with Woolsey. In every recent contribution to the subject of fractures, if the details of treatment are mentioned, early massage and passive motion are recommended, but no authorities agree with Championnière in discarding splints. There must be some form of dressing which will retain the fragments in their corrected position. In many fractures this treatment is quite simple, in others it is much more difficult, and should be performed by the surgeon responsible for the result. In a few words the method is as follows: At each dressing the leg should be carefully bathed, first, with very warm water, then with alcohol; the skin should be rubbed with the hands covered with some oily substance, cocoa butter is the best; the muscles of the limb should be gently manipulated, the degree of manipulation is in inverse proportion to the tendency to displacement and in direct proportion to the time since the injury. During the manipulation the fragments should be held in firm position by an assistant. In fractures in the neighborhood of joints early passive motion is of the greatest importance. At first it is given gently, and is increased with the time since the injury. The patient should be encouraged to exercise voluntarily the muscles of the affected extremity. With this method of treatment instituted early the results of fractures are decidedly improved. It unquestionably hastens bony union. When bony union is complete the joints are supple, the muscles are not atrophied, and the function of the limb is almost as good as before the fracture. After the older methods of treatment there was always a period after the union of the fracture and the removal of the dressing during which the function of the limb was greatly impaired, and, in many instances, especially in old people, the joints were more or less ankylosed permanently. In all fractures in which massage and passive motion are possible at an early period after the injury (seven to fourteen days) the function of the limb should be almost completely restored simultaneously with bony union. I believe that this method of treatment is very much neglected in this country.

The Early Operative Treatment of Uncomplicated Simple Fractures. With our experience that the danger of infection is almost eliminated when proper operative technique is maintained, many surgeons in recent years have practised and advocated immediate operation for the reduction and suture of recent simple fractures. This view has been supported by the X-ray findings, which have demonstrated that

perfect reduction is frequently not accomplished. The subject has recently been carefully reviewed by Völcker,[1] Rothschild,[2] and Lessing.[3] These three articles give us a very complete résumé of the subject up to date. The results of the non-operative treatment demonstrated that it is ridiculous and unnecessary to operate in every case of recent fracture. Operative intervention is indicated when complete reduction is impossible, especially if there is a dislocation of one fragment. This is especially true of fractures near joints in which the smaller fragment is dislocated and cannot properly be reduced without the open incision. It is also true of many transverse epiphyseal fractures. Unquestionably in these forms of fractures our results will be greatly improved by the early operation. In some instances we can easily decide for operation after the attempt at the reduction has failed without the use of the X-ray. In the majority of cases, however, on account of the small size of the fragment and its deep position, we can only be certain of its dislocation by the use of the X-ray. It is not necessary to operate at once. In many cases it is even better to delay a few days to allow the soft parts to get over the effects of the contusion. The results are frequently good when there has been delay of two to three weeks, but in the majority of these fractures operative interference within the first few days always gives better results.

On the other hand, in fractures in the shaft, and in many fractures near the joints in which the X-ray demonstrates perfect or even fair approximation, an operation is unnecessary. Recent experience has shown that there are objections to the operation. There are the dangers and complications of the anæsthesia which increase with the age and condition of the patient. If the fracture is deep seated, the manipulation of the soft parts necessary for the exposure of the bone unquestionably increases the danger of infection, which is present to a certain degree even with the most careful technique. For this reason, in fractures so situated one should have ample justification for the early operation. We have also found that the exposure of the fracture does not allow in every case a perfect approximation. This is due to the splintering and the irregularity of the ends of the fragments. Here perfect approximation could only be accomplished by resection, which should never be done in a recent fracture. The disturbance of the periosteum in the manipulation during the operation is always associated with delayed union. These objections are sufficient to influence our decision against operation, except in those cases in which the dislocation of one or both fragments, or the peculiarity of the line of

[1] Beiträge zur klin. Chirurgie, 1902, Band xxxiv. p. 624.
[2] Ibid., 1900, Band xxix. p. 245.
[3] Archiv f. klin. Chirurgie, 1902, Band lxviii. p. 222.

fracture (spiral fractures and certain comminuted fractures) in which we know that proper reduction and approximation are practically impossible without operation. The interposition of soft parts is a definite indication for operation. The consensus of opinion favors early operation in recent fractures of the patella and the olecranon. When we decide, for sufficient and definite reasons, to operate in a case of recent fracture we cannot be too careful of our technique; we should avoid undue and rough manipulation of the soft parts, and the greatest care should be taken to preserve periosteal attachments of the bone at the seat of fracture. After reduction the fragments should be held in position by suture; silver wire is preferred.

The Treatment of Delayed Union in Fractures. Now and then, although the fragments are in good apposition, solid bony union is delayed. When this is observed everything should be done to improve the circulation of the limb; more energetic massage, and if not already instituted, the ambulatory treatment. Recently the method advocated by Bier in the treatment of tuberculosis of joints, that is, venous obstruction produced by an elastic ligature, has been employed advantageously, both in delayed union in recent fractures and in delayed union after resection and suture in old, badly united fractures. This method was introduced in 1875 by Nicoladoni. The best method was introduced by Helferich[1] in 1886, and is again advocated by him in his recent text-book.[2] Fig. 8 illustrates Helferich's method. The extremity is encircled with a flannel bandage except at the seat of fracture. At the proximal end of the flannel bandage the limb is encircled with an elastic band placed sufficiently tight to produce venous but not arterial obstruction. Clinical experience demonstrates the value of this method. Recently, Bum,[3] from the Institute of Experimental Pathology, in Vienna, has demonstrated experimentally on animals that the development of bone in callus after fracture is increased under the influence of venous obstruction. The periosteal bone formation is chiefly stimulated. We have, therefore, the laboratory confirmation of the clinical observation.

FIG. 8.

THYROID MEDICATION IN THE TREATMENT OF DELAYED UNION OF FRACTURES. Murray,[4] of New York, reports a number of cases, and discusses the literature which dates from 1897. There is sufficient evidence to justify its use.

[1] Archiv f. klin. Chirurgie, 1887, vol. xxxvi.
[2] Loc. cit.
[3] Archiv f. klin. Chirurgie, 1902, Band lxvii. p. 652.
[4] Annals of Surgery, 1900, vol. xxxi. pp. 695 and 742.

The Ambulatory Treatment of Fractures. Helferich,[1] in his recent text-book, criticises this method as follows: "The ambulatory method may yield good results in important fractures of the lower extremity, but the technique of applying the cast is difficult, and the dressing requires constant careful supervision as long as it is worn; in other words, the danger of complications interrupting the course of recovery is greater in the ambulatory than in any of the other methods in ordinary use. On the other hand, the ambulatory method has the following advantages: Inflammatory diseases of the respiratory organs, such as bronchitis or hypostatic pneumonia, are rarer even in old subjects; delirium tremens even is said to be less likely to develop; it is the best means of avoiding atrophy of the muscles and rigidity of the joints; the callous formation is abundant, and it is said that insufficient callous formation is very rare when this method is employed. While some authorities reject the ambulatory method altogether, and others use it as soon as possible after the injury, I often follow the middle course in my clinic. After the swelling has subsided and the fragments are in good position, a firm bandage is applied and the patients are allowed to walk about at the end of the second or third week. At the beginning the pain of putting the foot to the ground will be materially lessened if some form of walking apparatus, like the 'walking chairs' of children, is employed."

I have given this opinion in full because Helferich is a recognized authority on fractures, in Germany, where this method of treatment originated and is chiefly employed. Scudder[2] holds practically the same opinion as Helferich, and also gives a very good résumé of the literature. I believe, however, that the introduction of the so-called ambulatory treatment of fractures has had a good influence and can be used in a modified form by the general practitioner. In fractures of the upper extremity only those confined to the upper end of the humerus require the extension treatment, which is more easily accomplished with the patient in bed. However, an ambulatory extension apparatus for fractures of the upper end of the humerus is not very difficult to apply, and should be used always in older people. In fractures of the lower extremity the problem is a more difficult one. In fractures below the knee no special apparatus is necessary, and I believe experience demonstrates that at least after the first or second week fractures below the knee do better if the patient is allowed to walk on crutches in a properly applied plaster-of-Paris bandage. If the fracture is above the middle third of the leg the bandage should extend at least to the middle of the thigh fixing the knee-joint. In fractures of the lower end

[1] Loc. cit., p. 73.
[2] The Treatment of Fractures.

of the femur, in the majority of cases, it is better, at least for the first two or three weeks, to dress the fracture in a flexed position. During this time the patient should be in bed. Later, when the fully extended position is maintained, there is no contraindication to allow the patient to walk on crutches with the entire lower extremity and hip fixed in plaster. In fractures of the shaft of the femur the difficulty of the ambulatory treatment is the apparatus. Even with the most improved and expensive special forms of apparatus the dangers of malposition are too great to allow its use except in the most experienced hands. In fractures of the upper end of the femur and the neck the dangers are even greater.

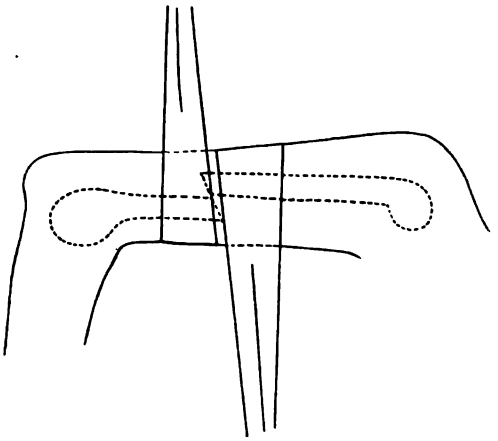
Nevertheless, I feel that in some fractures of the shaft and upper end of the femur the ambulatory treatment would give better results. The question to be solved is a simple and absolutely safe dressing.

The Use of Plaster in the Treatment of Fractures. Helferich[1] criticises the general use of plaster as a first dressing in recent fractures, and prefers splints. Later in the treatment, after the swelling in the seat of fracture has subsided, Helferich recommends the use of plaster. "Especially," he writes, "it is particularly useful, in view of the modern treatment by frequent massage at the seat of fracture, when it is cut down on each side and separated into two gutters, which are easily fastened together with strips of adhesive plaster and secured with a few turns of a roll of bandage." Scudder[2] gives us beautiful illustrations of the methods of applying the plaster dressing to various fractures, and the making of removable plaster casts. Stimson[3] writes that it may occasionally be used as a primary dressing if very carefully watched. It is the consensus of opinion that one inexperienced with the treatment of fractures and in the use of plaster-of-Paris should never use this as a first dressing. On the other hand, I believe, as we become more experienced, we use plaster-of-Paris more frequently as a primary dressing. The chief danger of the plaster-of-Paris dressing is from pressure. This, however, can always be avoided by proper padding. In applying the plaster-of-Paris dressing to many fractures the danger of a recurrence of the dislocation of the fragments during the application of the dressing is greater than in other forms of fracture dressings. Bähr[4] advocates a very useful device to hold the fragments in apposition during the application of the dressing, especially useful when plaster-of-Paris is used. Fig. 9 illustrates the method better than a detailed description. I have found it very useful and convenient in fractures of the shaft. The ends of the traction band come out through

[1] Loc. cit. [2] Loc. cit. [3] Loc. cit.
[4] Centralblatt f. Chirurgie, 1901, Band xxviii. p. 321.

a window in the plaster. Before completion of the dressing they can be included in the last rolls of the plaster bandage, or, if we wish to exert the correcting traction later, the bands can be tied over a piece of splint. Codman,[1] of Boston, advocates and illustrates a similar method

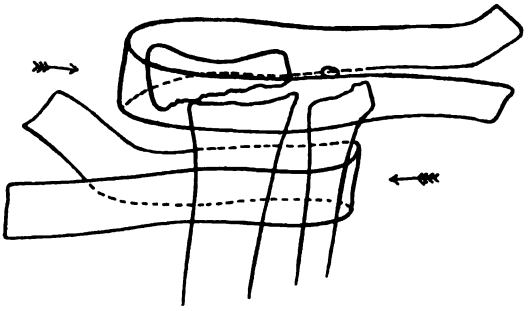
FIG. 9.



in Colles' fracture to control the tendency of the hand to become displaced to the radial side, as shown in Fig. 10.

Conclusions as to Treatment of Fractures in General. We may sum up and emphasize the following points: The proper reduction of the fracture by operation, if necessary, the application of as simple a

FIG. 10.



Cross-traction method for Colles' fracture.

dressing as possible, which will retain the fragments in their corrected position, confirmation of the corrected position by the X-ray, constant supervision to prevent secondary deformities, frequent dressings, to allow early massage and passive motion, the introduction of the ambulatory

[1] Boston Medical and Surgical Journal, 1900, vol. cxliii. p. 307.

treatment as soon as possible, the early recognition of delayed union, and the introduction of more radical measures to stimulate the development of osseous tissue in the callus as venous obstruction, thyroid medication, more energetic massage, and the ambulatory treatment, the latter, even with the risk of some resultant deformity.

Special Fractures. One is surprised at the rather voluminous literature on fractures during the last two years, especially on the treatment of recent simple fractures. The impetus to this is undoubtedly due to the introduction of the Roentgen rays. Nevertheless, it must be considered a positive indication of the dissatisfaction with the results in our treatment of fractures. Certain fractures stand almost alone, because of their very common bad results after our ordinary treatment. Fractures at the lower end of the radius and fractures about the elbow-joint are given the chief consideration. Various epiphyseal fractures rank next. In going over the fractures admitted to the surgical clinic of the Johns Hopkins Hospital, because of the bad result from the treatment in their recent state, Colles' fractures are the most numerous, and flat-foot, following Pott's fracture, next. Epiphyseal fractures, fractures in the neighborhood of joints and of the shaft of long bones, appear to be equal in number. We seldom observe cases of non-union when the fragments are in good position. These old cases of fracture come to the surgical clinic because of union with deformity. Studying the cases in detail, we find that a small proportion of the cases were not recognized nor treated in the recent state. The larger number, however, were recognized, and the faulty position was due, not to improper treatment, as far as the application of the dressing, but to incomplete reduction at the first treatment, which was not recognized, or, at least, not corrected until bony union had taken place. From the reading of the literature and this experience, I feel convinced that the chief fault in the treatment of fracture in the majority of instances is due to imperfect reduction, which frequently cannot be recognized without the use of the X-ray. In the majority of instances anæsthesia is necessary for reduction. If the X-ray shows that this is not accomplished the operation should not be delayed.

Fractures of the Upper End of the Humerus. Lorenz[1] reports the very rare isolated fracture of the small tubercle (tuberculum minus humeri), with a discussion of the few cases in the literature. When these fractures are isolated, as in Lorenz's case, they are probably tear fractures. This patient, a male, aged forty-five years, received a severe wrench, producing forced outward rotation when the arm was in a position of adduction and outward rotation. The man experienced

[1] Deutsche Zeitschrift f. Chirurgie, 1901, Band lviii. p. 593.

acute pain in the region of the shoulder-joint and heard a distinct noise. There was no dislocation. There was some swelling, and in a few days localized ecchymosis — a very important point in the diagnosis of fracture due to indirect force. The fracture was not recognized in the recent state, and the patient was refused any benefit from his accident policy from the medical examiner, who failed to find the nature of the injury. Lorenz saw the patient sixteen months after the injury. The symptoms were characteristic. The patient was unable to place the hand of the affected right side behind his back, or put the right hand in his trousers pocket, as shown in Fig. 11, without the aid of his other hand, that is, the internal rotation was practically impossible. Outward rotation, as shown in Fig. 12, was increased 40°. Other motions of the shoulder-joint were not impaired. There was nothing to be seen on inspection.

FIG. 11.

FIG. 12.

On palpation a sharp edge of bone was felt at the position of the minor tubercle, and a loose piece of bone below the coracoid process. The

injury was easily explained. In forced outward rotation the over-extended subscapular muscle had produced a tear fracture at the point of its insertion on the minor tubercle. In the recent state such a tear fracture should be treated by forced inward rotation, that is, the fixation of the arm with the forearm behind the back. If union does not take place, one should operate. Lorenz's patient refused operation. In this case, if the patient's arm has been in abduction rather than adduction, he would probably have sustained a dislocation, and, perhaps, with the same tear fracture, which is not so very uncommonly associated with the dislocation.

Fractures of the anatomical neck and epiphyseal separations of the upper end of the humerus are rather difficult fractures to recognize and to treat. When the dislocation of the upper fragment can be reduced, and the proper reduction is confirmed by the X-ray, operation is not indicated; but the extension treatment advised by Helferich[1] should be employed, with the arm in a slightly abducted position. The neglect of this method is frequently associated with union with more or less deformity. When the fragment is dislocated and reduction impossible, one should resort to early operation. Curtis,[2] of New York, reports three cases, and compares the results after reduction or resection in twenty-five cases with the conclusion that reduction, if possible, gives the most satisfactory results, and states that even a delay of one to four weeks will not impair the results. Resection is only indicated in older fractures or those in which reduction is impossible. The entire subject of epiphyseal separation of the upper end of the humerus is considered by Linser.[3] He bases his conclusions on twenty-two cases from the surgical clinic of von Bruns in Tübingen. He agrees with Helferich that the extension treatment gives better results than the older method of fixing the arm in the Velpeau position. If the fragment cannot be reduced, or when it is found later to have united in a faulty position, he recommends operation, agreeing with Curtis to reduce if possible. Lessing[4] in his article on the "Early Operative Treatment of Uncomplicated Intra-articular and Para-articular Fractures" mentions the fractures under discussion among those in which early operation is indicated, if perfect reduction is not accomplished. The patient, a woman, aged thirty-three years, appeared at the surgical clinic ten days after the injury, with the diagnosis of an outward dislocation, for which attempts at reduction had been made. The deformity, however, was typical of a fracture of the surgical neck, the arm was greatly abducted, the upper end of the lower fragment could be felt in the

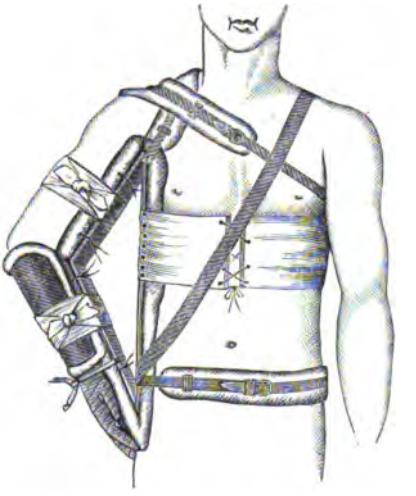
[1] Loc. cit. [2] Annals of Surgery, 1900, vol. xxxi. p. 291.
[3] Beiträge zur klin. Chirurgie, 1900, Band xxix. p. 350.
[4] Loc. cit.

axilla, and the upper fragment could be palpated beneath the acromial process. The illustration shows an unusual dislocation of the upper fragment, impossible to reduce without operation. In this case the operation was successful in reduction, and the functional result perfect.

EXTENSION IN FRACTURES OF THE UPPER END OF THE HUMERUS AND OBLIQUE FRACTURES OF THE SHAFT. In these cases if the deformity can be properly reduced it is unnecessary to operate, but I believe that the treatment by extension will yield better results. This method of treatment is not often used in this country. It is not specially recommended by Scudder[1] in his recent book, nor by Stimson.[2] Helferich, however, advises it. In the majority of instances this extension can be applied very simply, as shown in Fig. 13. I believe this

FIG. 13.

FIG. 14.



form of extension should be combined with the usual triangular pad in the axilla, and the arm fixed to the side of the body with the usual bandage. In this apparatus the patient can be up and about during the day, and at night the extension can be maintained by a simple pulley. In other cases it is necessary to have the arm in a marked abducted position, in order to retain the fragments in proper apposition. Middeldorpf's triangle, illustrated in Fig. 14, is a very excellent and convenient dressing. This, however, in some cases should be combined with extension. Sultan[3] has recently devised a very convenient apparatus for combining Middeldorpf's triangle with extension, as

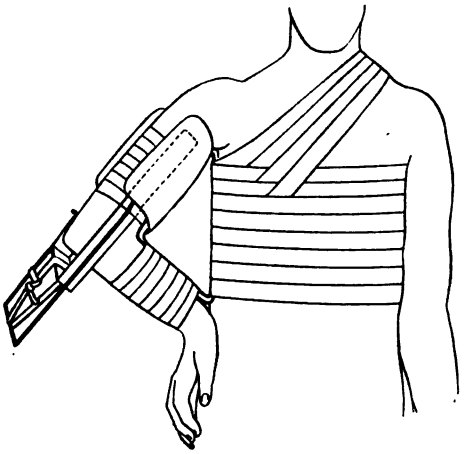
[1] Loc. cit.

[2] Loc. cit.

[3] Archiv f. klin. Chirurgie, 1901, Band lxiii. p. 757.

shown in Fig 15. The illustration hardly needs an explanation. The triangle can be made of pasteboard, strengthened with adhesive straps and properly padded. The extension is accomplished by the ordinary adhesive plaster on the skin attached to the usual square piece of board. In the dressing on the arm one should incorporate a bent piece of metal splint, which should extend a few inches beyond the piece of board. Between the board and the metal splint an elastic tube makes the extension. I would urge the more general use of extension in these fractures of the humerus and its combination with abduction in those cases in which tendency to displacement of the fragments is less than in the straight position.

FIG. 15.



FRACTURES IN THE NEIGHBORHOOD OF THE ELBOW-JOINT. Our results in the treatment of these fractures are unusually unfortunate, and there is considerable difference of opinion with regard to the method of treatment. Frederick J. Cotton,[1] of Boston, has contributed the most exhaustive and satisfactory study of these fractures. The conclusions based on his own experience and the most careful study of the literature are as follows: The outcome under any of the ordinary methods of treatment very rarely gives complete ankylosis, and the loss of motion is pretty accurately in inversed proportion to the accuracy of reposition; that is, the fundamental principle in the treatment of all fractures (proper reduction) is perhaps of greater importance in these special forms of fractures than in any other. The second point of importance is the position of the forearm—full extension, forced flexion,

[1] Annals of Surgery, 1902, vol. xxxv. pp. 75, 242, and 365.

or at some medial position. This position should vary with the variety of fracture. In *fractures of the external condyle*[1] of the humerus, reduction is best accomplished by flexion and pronation with lateral pressure on the fragments, and this fracture should be dressed at an acute angle flexion. The deformity following this fracture, according to Cotton, is not the varus or the valgus, but an outward or outward and backward displacement of the condyle, with or without displacement of the ulna, and a spur formation above the condyle. The deformity is

FIG. 16.

FIG. 17.

associated with limitation of extension, and can be prevented best by reduction in the manner described above, and retention in forced flexion. In *supracondylar fractures* and *epiphyseal separations* reduction is best accomplished by traction in a flexed position, and this position should be maintained in a right-angle splint. To prevent the forearm from slipping backward this splint should be fixed with adhesive straps, with a small pad at the bend of the elbow for counter-pressure. In this fracture we must guard against backward displacement of the lower fragment of the humerus, which if not corrected will limit flexion at the elbow, and backward rotation, and if not remedied

[1] Cotton's nomenclature.

gives rise to the varus deformity. The position of acute flexion should not be used in supracondylar fracture and epiphyseal separation. The varus deformity, according to Cotton, is best prevented by full extension of the forearm; but this position is unwise because of the greater opportunity of backward displacement of the lower fragment. The latter deformity is the worse of the two evils. However, we can correct the tendency to the varus deformity by gradual extension after the second week. Therefore, in fractures above the condyles and epiphyseal separation we first fix the forearm at a right angle, after the

FIG. 18.

FIG. 19.

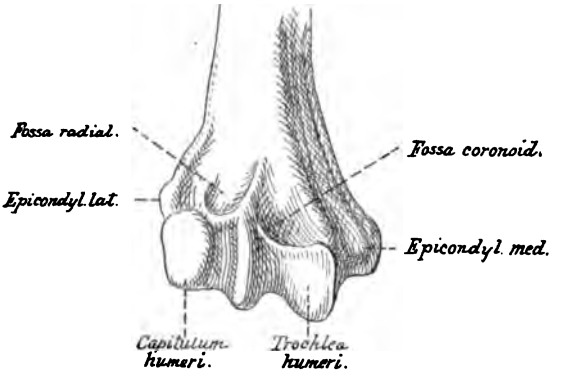
second week and at each subsequent dressing we increase toward the position of full extension. In *epitrochlear separations and fractures* (internal epicondyle) the best results are obtained by the position of forced flexion. However, in this fracture the prospect for bony union is poor, and for this reason Cotton recommends early massage and passive motion.

As to the operative treatment of these fractures—first, in their recent state, because of the irreducibility of a fragment, or later for the deformity—Cotton writes that it is yet too early to give very definite indications. Figs. 16, 17, 18, and 19 very graphically picture the

proper method of the treatment of fractures of the internal epicondyle, internal condyle, the external condyle, and T-fractures at the elbow-joint.

CLASSIFICATION OF FRACTURES AT THE ELBOW-JOINT. The terminology to distinguish the different fractures at the lower end of the humerus is frequently misleading, especially in English. According to Helferich[1] these fractures do not lend themselves to classification,

FIG. 20.



but present a great variety of forms which often merge into one another. Even the anatomical terms used in describing the lower end of the humerus are frequently not uniform. I should advise the adoption of the modern terms advocated by Spalteholz.[2] Fig. 20 gives the revised nomenclature.

FIG. 21.

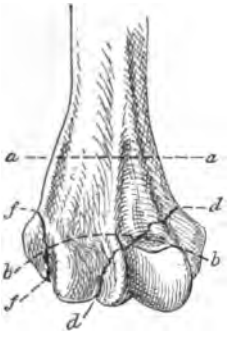


FIG. 22.

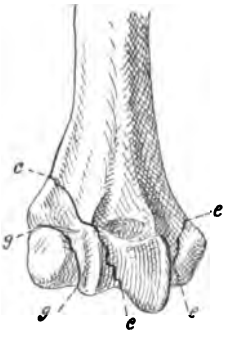


FIG. 23.

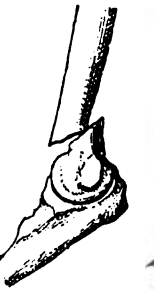


FIG. 24.

Helferich describes the following fractures of the lower end of the humerus, illustrated in Figs. 21 and 22.

1. *Fractura Supracondylica.* (Supracondylar fracture.) (See *a-a*, Fig. 21.) This fracture may be transverse or oblique. It may occur

[1] Loc. cit., p. 173.

[2] See the American edition of this Atlas of Anatomy, recently translated by Barker.

both before or after the ossification of the epiphysis. It is always above the epiphyseal line, and in the majority of instances the lower fragment is dislocated posterior with the forearm. This form has been designated by Kocher[1] as the extension supracondylar fracture, and is well illustrated in Fig. 23. Exceptionally the line of fracture does not allow the posterior dislocation of the lower fragment. Then we have the so-called flexion fracture of Kocher, as shown in Fig. 24. The flexion fracture is usually produced by a fall on the elbow, while the extension fracture is caused by a fall on the palm of the hand when the forearm is fully extended.

2. *Fractura Processus Cubitalis s. Articularis; Fractura Diacondylica.* (Transverse fracture of the true articular process.) (See *b-b*, Fig. 21.) We must remember that the lower epiphysis of the humerus unites with the shaft about the seventeenth year. This epiphysis is made up of the coalesced nuclei of the external epicondyle, capitellum, and trochlea. This fracture, therefore, before the seventeenth year is a true epiphyseal separation; later a fracture. As a fracture it is a rare injury. It is always a true intra-articular injury.

3. *Fractura Obliqua Externa; Fractura Condyli Externi.* (The external oblique fracture). (See *c-c*, Fig. 22.) This is usually called a fracture of the external condyle. The term, however, is not known to anatomical nomenclature. Before the eighth year we can have an epiphyseal separation of the external epicondyle. After the eighth year this nucleus unites with the capitellum, so that between the eighth and thirteenth year we may have a separation of the external epicondyle and the capitellum together; so that the so-called fracture of the external condyle is an oblique fracture of the lower end of the humerus, carrying with it the epicondyle and capitellum. It always extends into the joint. According to Cotton and other authorities, it is the most common of elbow fractures in children.

4. *Fractura Obliqua Interna; Fractura Condyli Interni.* (The oblique internal fracture of the lower end of the humerus.) (See *d-d*, Fig. 21.) This fracture, frequently incorrectly called fracture of the internal condyle, is an oblique fracture of the lower end of the humerus, extending into the joint, including the internal epicondyle and trochlea. It can never be a true epiphyseal separation, and as a fracture it is very rarely observed.

In very exceptional cases we may have a double oblique fracture.

5. *Fractura Epicondyli Interni; Fractura Epitrochleæ.* (The fracture of the internal epicondyle.) (See *e-e*, Fig. 22.) This is frequently incorrectly called a fracture of the internal condyle, while it should be

[1] PROGRESSIVE MEDICINE, December, 1900, pp. 140, 141.

designated as epicondyle or medial condyle. It is one of the common fractures of the lower end of the humerus. As the nucleus of the internal epicondyle does not unite until the eighteenth year, this fracture up to this age is an epiphyseal separation, and is not an uncommon injury. It is usually a tear fracture, and is generally associated with outward dislocation.

6. *Fractura Epicondyli Externi; Fractura Epicapituli.* (The fracture of the external epicondyle.) (See *f-f*, Fig. 21.) This very rare injury should be called a fracture of the external epicondyle or lateral condyle, and not of the external condyle. As an epiphyseal separation it is possible only up to the eighth year.

7. *Fractura Rotulare Partialis; Fractura Processus Articularis Partialis.* (The intra-articular fracture separating the capitellum humeri.) (See *g-g*, Fig. 22.) This fracture of the capitellum is entirely intra-articular. It is a very rare injury. It is possible as an epiphyseal separation up to the eighth year only. According to Kocher, the fragment can be felt between the external epicondyle and the head of the radius when the arm is in extension. It may be mistaken for a fracture of the head of the radius. The fragment should be removed.

8. *Fractura Intercondylica; Fractura Condylo-intercondylica.* (Longitudinal and T-fracture of the lower end of the humerus.) These are very severe injuries, like the double oblique fractures just mentioned (fractura condylica), are not infrequently compound fractures, and very difficult injuries to treat. According to Scudder, they should be treated in flexion; according to Helferich, in extension. In my observations oblique internal fractures of the lower end of the humerus are not infrequently considered T-fractures.

Helferich does not mention the possibility of an isolated separation of the trochlea similar to the capitellum. It is possible, but rare.

According to Cotton,[1] the frequency of these lesions of the elbow-joint is as follows: 1. External condylar fractures; that is, the oblique external fracture or the epiphyseal separation of the external epicondyle and capitellum. 2. Supracondylar fractures. 3. Epitrochlear separations; that is, the separation of the internal or medial epicondyle. 4. Epiphyseal separation of the whole lower epiphysis. Other fractures are very rare. The frequency and the X-ray photograph of epiphyseal separations of the lower end of the humerus have been fully considered in the December number of PROGRESSIVE MEDICINE, 1900.

TREATMENT OF FRACTURES OF THE LOWER END OF THE HUMERUS. When these fractures of the lower end of the humerus are associated

[1] Loc. cit., p. 396.

with a good deal of joint effusion and swelling we should use for the first few days a temporary dressing, fixing the arm in the most comfortable position, usually at a right angle. When this swelling has somewhat subsided the patient should be etherized and the fragments, if possible, properly reduced. Supracondylar fractures and separation of the lower epiphysis of the humerus should be dressed with the forearm at about a right angle. The single and double oblique fractures and fractures of the epicondyles should be fixed with the forearm in forced flexion. When the X-ray shows that the fragments are not properly reduced an early operation, with reduction and suture, is indicated.

FRACTURE OF THE CORONOID PROCESS OF THE ULNA. This is usually considered a rare fracture, and is frequently overlooked. The fracture is not mentioned by Scudder.[1] Helferich[2] mentions it but briefly, with one illustration only. (Fig. 25.) This illustration does not give one a proper idea of the fracture. Helferich, however, calls attention to its rarity, and that it is usually observed with a backward dislocation of the forearm at the elbow, and to the anatomical fact, frequently overlooked, that the brachialis anticus muscle is not attached to the tip of the process, but to the base, so that if the tip only is fractured the fragment is not acted upon by this muscle. In this fracture we arrive at the diagnosis frequently by exclusion. By palpation we can exclude fractures more commonly observed in the elbow-joint. Yet the symptoms of a severe joint injury indicate a fracture. The fragment cannot always be palpated. But these symptoms of a joint injury, associated with the exclusion of the other possible fractures, and especially if associated with the possibility of pushing the forearm backward, make one suspicious of a fracture of the coronoid process. Now and then, in pushing the arm backward and drawing it forward, we may elicit crepitus. This fracture alone must be a rare injury. In the surgical clinic of the Johns Hopkins Hospital we have observed but one positive case exhibiting the symptoms just described. We were unable to feel the fragment or to elicit crepitus.

FIG. 25.

[1] Treatment of Fractures. Philadelphia, 1900.

[2] Loc. cit.

The treatment followed was that recommended by Helferich. The forearm was drawn forward and fixed in acute angle flexion, massage and passive motion were done early, with an excellent result. Stimson,[1] in his recent treatise, pictures a fracture of the coronoid process and the head of the radius. (Fig. 26.) Carl Beck,[2] in a recent observation of three cases, is inclined to believe that the fracture is more common than usually supposed, and is frequently overlooked because associated with other injuries, such as a posterior or lateral dislocation at the elbow or a fracture of the olecranon process or radius.

FIG. 26.

Beck's first case was observed as a recent accident. The patient, a male, aged forty-six years, very stout, fell on the extended forearm on the ulnar side of the hand. The clinical picture was that of a fracture of the olecranon process. The X-ray photograph, however, demonstrated that there was also a fracture of the coronoid process. Beck was able to reduce the fragments without anæsthesia, and an excellent result was obtained, first by fixation in the fully extended position, and later in the flexed position.

Beck's second observation shows a typical fracture of the coronoid process, healed with slight outward dislocation, associated with an outward dislocation of the radius, demonstrating the combination of this fracture with a dislocation of the radius. This patient was not observed by Beck until two years after the injury. There had been a direct trauma to the elbow-joint, the patient's arm having been caught in the strap of machinery. The injury had been diagnosed and treated as a fracture of the upper end of the radius. The result was paralysis of the forearm and fixation of the elbow-joint at an acute angle. The dislocation of the radius and the coronoid process probably compressed the musculospiral nerve. So we have a combination in this case of three injuries, all overlooked in the recent state. A proper diagnosis and treatment in this case unquestionably would have given a different result. Beck recommended a chiselling of the dislocated coronoid process and excision of the head of the radius.

In Beck's third case the patient was a male, aged fifty years, and the injury—a compound fracture at the elbow-joint—of eleven years' duration; the wound was some months in healing, and left the joint ankylosed and in acute flexion. During the last few years the patient suffered a good deal of pain and tenderness about the ankylosed

[1] A Practical Treatise on Fractures and Dislocations. Philadelphia, 1899.
[2] Deutsche Zeitschrift f. Chirurgie, 1901, Band lx. p. 193.

elbow-joint; the Roentgen photograph, according to Beck, shows a healed fracture of the coronoid process dislocated laterally; also a great deal of new bone formation about the fracture, with the olecranon fixed to the external condyle. There was new bone formation about the external condyle; the changes in the joint surfaces, due to arthritis deformans—the result, no doubt, of infection—make the picture a rather complex one, and I do not believe they are a positive index to the original injury.

I have observed one case which, I think, is quite analogous to Beck's first observation. The patient was a boy, aged nineteen years. Five

FIG. 27.

months previous to my first examination the patient's left elbow had been caught in machinery and severely wrenched; it was treated for a fracture of the olecranon; result, partial ankylosis.

Examination. The forearm could be extended to twenty-five degrees of full extension; from this point it could be flexed only twenty degrees; pronation was not restricted; supination was possible only to a point midway between complete pronation and complete supination; the head of the radius was not dislocated; there was a large mass of callus over the ulna on its anterior surface, extending over the internal

epicondyle of the humerus. It was this mass of callus which seemed to prevent flexion. On the posterior surface of the ulna there was an obtuse angular deformity toward its flexor surface; the apex of the angle corresponded about to the position of the base of the coronoid process; there was no motor paralysis, but an area of anæsthesia confined to the distal phalanx of the index and the middle finger, demonstrating that the filament of the median nerve must have been caught in the callus. Fig. 27 is an X-ray photograph taken from the ulnar lateral side. We see at once that there is a fracture of the olecranon process, partly united by bony and partly by fibrous union, at an obtuse angle with the shaft of the ulna. The position of the coronoid process is represented by a very large mass of callus; the radius and humerus are normal. I do not see how this mass of callus in the position of the coronoid process can be explained by the fracture of the olecranon process only. Fig. 28 is an X-ray photograph of the elbow taken from behind. The line of fracture in the ulna is not shown; it is probably obliterated by the partial bony union. The callous tumor is seen first in the widening of the shadow of the ulna and the lighter shadow to the medial side of the internal condyle and olecranon process.

FIG. 28.

Operation. Under anæsthesia the range of the possible elbow motion was not increased. The incision was made on the anterior (flexor) surface of the elbow to the ulnar side of the median nerve. There was some scar tissue about the muscles and around the median nerve. The pronator radii teres muscle was divided. This exposed the callus tumor. There was a small piece of new bone adherent to the sheath of the median nerve. The callous tumor corresponded to the coronoid process. The line of fracture seemed to have been oblique, so that the coronoid process and part of the shaft of the ulna had slipped slightly upward, producing the angular deformity mentioned. The callous tumor was about four times the natural size

of the coronoid process. Bone was removed until complete flexion at the elbow-joint could be made without force. It was considered best not to refracture and correct the angular deformity of the shaft of the ulna. The wound was closed and the arm dressed in forced flexion. Passive motion was begun at the end of the week. It was six months or a year before complete motion of the elbow-joint was re-established. At this time, something more than two years since operation, the functional result at the elbow-joint is almost perfect. The area of anæsthesia disappeared; the arm is as strong as the other.

FRACTURES AT THE LOWER END OF THE RADIUS, INCLUDING COLLES' FRACTURE. Recent literature agrees fully with the emphatic statement of John B. Roberts,[1] of Philadelphia, made some years ago, that reduction is the most important factor in the treatment of these fractures, and that impaction of the fragment is no contraindication for the breaking up of the impaction and correcting the displacement when present. Roberts writes that he has "never learned to expect to see the fracture completely reduced by resident physicians or general practitioners." A study of the literature and my own experience agree with the following conclusions of Dr. Roberts:

1. Fracture of the lower end of the radius is one of the most satisfactory of all fractures to treat.

2. The patient, as a rule, has little discomfort after the first twenty-four hours, except from the disability and the annoyance of the sling and dressing.

3. Stiffness of the fingers and wrist-joint is seldom present to any marked extent after a week.

4. Deformity after treatment is usually so slight as to be unnoticeable to the average observer, except in cases where there has been marked comminution of the lower fragment.

5. These assertions are only justified when the surgeon insists upon forcing the lower fragment into its proper anatomical relation with the upper fragment. This is to be done by the exercise of such a great amount of force as will break up all impaction or entanglement and bring the broken surfaces into accurate coaptation. This sometimes, but not usually, requires general anæsthesia; and may demand that the surgeon bend the broken bone across his knee in order to disentangle the interlocked fragments.

VARIETIES OF FRACTURES AT THE LOWER END OF THE RADIUS. It is of great importance to know that the line of fracture at the lower end of the radius takes various directions, and this fracture may be associated with a fracture at the lower end of the ulna (rare); a fracture

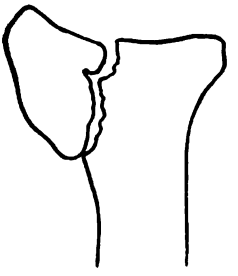
[1] Annals of Surgery, February, 1899; also, A Study of Fractures of the Lower End of the Radius. Philadelphia, 1898.

or separation of the styloid process of the ulna (common, 60 to 65 per cent.); a rupture of the interarticular triangular fibrocartilage at its insertion at the base of the styloid process of the ulna (very common); and a fracture of the scaphoid bone (uncommon) more frequently occurs alone.

In discussing the varieties of fractures I find it more satisfactory to use the contribution of Codman,[1] of Boston. This classification agrees with Kahleyss',[2] which has been adopted by Helferich,[3] and with the more recent contribution of Carl Beck,[4] of New York. Codman's classification is based on the skiagrams of 140 cases of fractures of the lower end of the radius treated at the Massachusetts General Hospital, and Beck's study on 123 cases.

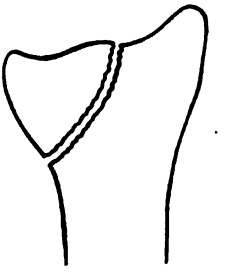
Class 1. (Fig. 29.) *Fractures from the Base of the Styloid Process to the Radius.* This is an oblique intra-articular fracture. This variety is illustrated by both Kahleyss[5] and Scudder.[6] It was observed

FIG. 29.



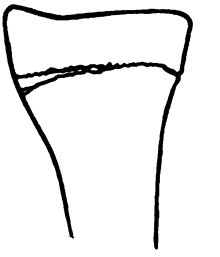
Fracture through base of styloid process.

FIG. 30.



Fracture through the inner angle.

FIG. 31.



Transverse fracture without displacement.

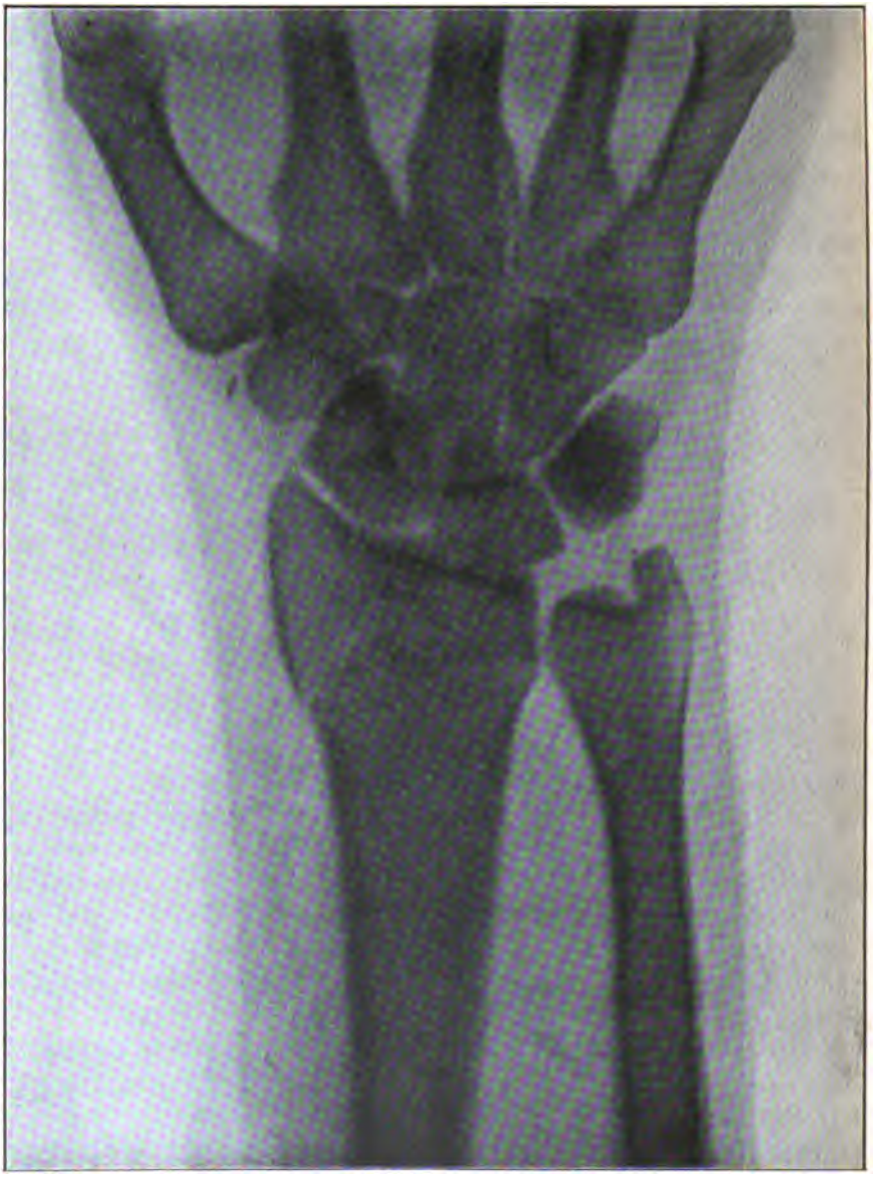
four times by Codman. In one case the styloid process of the ulna was also broken. It is a rare fracture, and not associated with any deformity of the hand or wrist. The fragment may be displaced slightly upward and backward by the supinator longus muscle. It should be easily recognized by the palpation of the fragment and the absence of the usual deformity. The fragment can be easily reduced and held in place by a strip of adhesive plaster. Beck[7] has not observed this fracture.

Class 2. (Fig. 30.) *A Fracture of the Inner Angle of the Lower End of the Radius.* Similar to Class 1, an oblique intra-articular fracture, illustrated also by Kahleyss and Scudder, but not by Beck. Codman observed three cases, in two the styloid of the ulna was broken.

[1] Boston Medical and Surgical Journal, 1900, vol. cxliii. p. 305.
[2] Deutsche Zeitschrift f. Chirurgie, 1897, Band xlv. p. 531.
[3] Loc. cit. p. 215.
[4] Annals of Surgery, 1901, vol. xxxiv. p. 245.
[5] Loc. cit.
[6] Loc. cit.
[7] Loc. cit.

It is associated with no deformity except slight increase in the circumference of the wrist. The fragment may be slightly dislocated back-

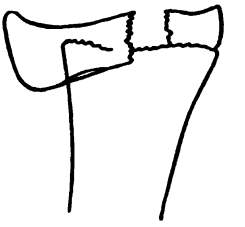
FIG. 32.



ward. It is easily replaced. There is subluxation of the ulna if the styloid is broken. This fragment should also be replaced. The injury can be dressed similar to Class 1, with the addition of a few splints.

Class 3. (Fig. 31.) *Transverse Fracture at or a Little Above the Epiphyseal Line* (in adults, without displacement). The line of fracture is similar to that observed in the ordinary Colles' fracture (see Class 8), except there is no displacement of the fragment, which sometimes is slightly impacted. Codman observed sixteen cases (11 per cent.). He states, however, that perhaps if he had made lateral views the skiagram would have demonstrated slight posterior displacement, and so placed some of these cases in Class 8. This variety of fracture is illustrated by Kahleyss and Beck. It is associated with practically no deformity. As a rule, crepitus can be elicited; 66 per cent. of these cases were associated with fracture of the ulnar styloid. This variety of fracture is, no doubt, frequently overlooked. It is beautifully illustrated by Beck. (Fig. 32.) The X-ray also demonstrates a transverse ulnar fissure in direct continuation of the radial fracture. There is also a fracture line in the scaphoid bone, illustrating the possibility of this associated injury mentioned before. It is very important in this variety of fracture to make a lateral view, and if there is posterior displacement of the lower fragment, the deformity should be reduced. One should also be quite certain that the fragment of the lower end of the ulna is replaced in proper position. This fracture needs but the simplest dressing, and unquestionably accounts for the many good results in the so-called Colles' fractures which have been treated without any attempt at reduction.

FIG. 33.



Commutation of distal fragments.

Class 4. (Fig. 33.) *Comminuted Colles' Fracture.* This variety differs from Class 8 only in the fact that the distal fragment is broken into two or more pieces. The classical deformity of the Colles fracture is always present. One fragment, however, may be displaced anteriorly; there may be impaction of the fragments. Codman has observed thirteen cases, 9 per cent. In every case the styloid process of the ulna was broken. The treatment of this variety is the same as that in Class 8 (Colles' fracture). Impaction, if present, should be broken up. Every effort should be made to replace the fragments of the radius and the lower end of the ulna. Perfect reduction is always difficult, frequently impossible. Even when properly treated the results are not always satisfactory. There is usually some deformity. This variety is illustrated by Scudder, Kahleyss, and Beck. Fig. 34, taken from Helferich, illustrates a very marked and typical deformity in *an old comminuted fracture of the lower end of the radius.* The shortening noted in Beck's case is present, and in addition there is a marked displace-

ment of the carpus to the radial side. It appears as if the styloid process had also been fractured and had united in an inverted position. This inversion of the styloid process of the ulna is illustrated by Beck (Fig. 35), the radial fragment, however, is in good position. The X-ray shadow of this healed fracture demonstrates that the line of fracture is through the inner angle of the lower end of the radius (see Class 2, Codman). In two of Codman's three cases the styloid process of the ulna was broken similar to this case of Beck's. In the latter's case it was associated clinically with intense pain in any effort at bending the wrist-joint. In the recent state it could have been easily replaced in the proper position. At this late period (eight weeks) the deformity

FIG. 34.

could be corrected and the pain relieved only by operation. Comminuted fractures of the lower end of the radius are, therefore, quite common, about third in frequency. With rare exceptions they are associated with fractures of the ulna or styloid process. The typical deformity of a Colles fracture is always present. Reduction is difficult, but according to Beck can be accomplished under anæsthesia. The reduction should always be confirmed by an X-ray examination within the first few days. If the X-ray shows that the fragments are not properly reduced a second attempt should be made under anæsthesia. I believe that this variety of fracture is accountable for the majority of bad results.

FIG. 35.

Class 5. (Fig. 36, *a b.*) *Separation of the Lower Epiphysis of the Radius.* Codman observed seventeen cases—*i. e.*, second to Colles' fracture in frequency. Fracture of the styloid process of the ulna occurred in all the cases in which this process was ossified (six out of seventeen cases). According to Codman, some of these cases showed no displacement of the fragment similar to Class 3 in adults. Others showed the typical Colles deformity. As a rule, reduction is simple, and there is little tendency to secondary displacement. Epiphyseal separation is, therefore, not uncommon. This is agreed to by Helferich and Scudder. According to the latter, there is usually less deformity than in the typical Colles. The treatment is the same. If there is a dislocation of the lower fragment, proper and complete reduction are very important. According to Beck, the deformity can seldom be recognized without a lateral X-ray view. This is beautifully demonstrated in Fig. 37. Here we see the line of fracture in the radial and

FIG. 36.

Separation of epiphysis.

ulnar epiphysis. This line was shown only by lifting the ulnar margin of the hand; a previous X-ray (not here reproduced) showed a normal shadow. The marked dorsal displacement in this case is shown in Fig. 38, a lateral view.

Class 6. (Fig. 39.) *Separation of the Epiphysis with a Chip off the Posterior Surface of the Diaphysis.* Codman observed this in ten cases, or 7 per cent. A fracture of the styloid process of the ulna was present in all of the cases except two; in these two the process was not ossified. The treatment is the same as in Class 5. Codman has, therefore, observed twenty-seven cases of epiphyseal separation—uncomplicated seventeen times, complicated ten times, demonstrating the frequency of this fracture. This variety is not illustrated or mentioned by the other authorities.

Class 7. (Fig. 40.) *Impaction of the Lower Fragment into the Shaft of the Radius.* Codman has observed this rare variety only twice. In one the styloid process of the ulna was broken, in the other case it

could not be determined positively. This fracture is associated with deformity, the relations of the styloid processes are altered, there may be posterior deformity, there is slight radial displacement, there

FIG. 37.

is no crepitus. In treatment the impaction should be broken up and the deformity reduced. This variety is not illustrated by other authorities.

Class 8. (Fig. 41.) *The Typical Colles Fracture.* Of Codman's 140 cases, 64, or 46 per cent., belong to this class. In 89 per cent. at

FIG. 38.

least the styloid process of the ulna was broken. Codman divides Colles' fracture into two forms: (*a*) Those in which radial displacement of the lower fragment is most marked, and (*b*) those in which

the posterior displacement of the lower fragment is most marked. In the former (the radial) the styloid process was always broken, in the latter (posterior) the styloid process of the ulna was not always broken. In all cases, however, both deformities are present to some extent. The amount of impaction varies in the individual cases. This variety

FIG. 39. FIG. 40.

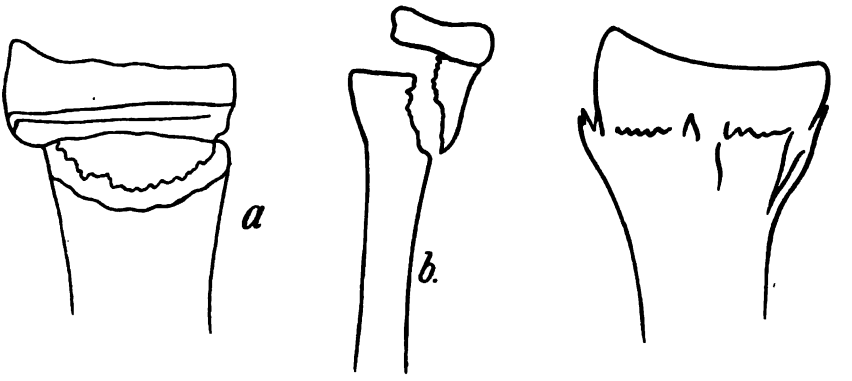
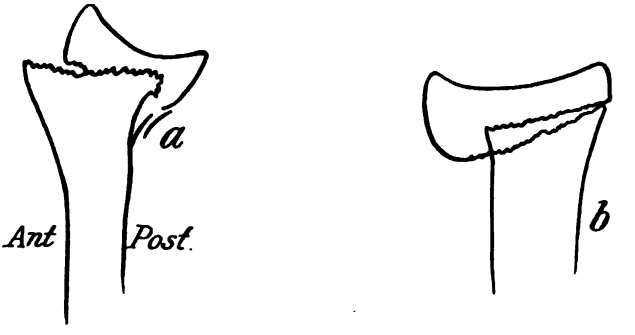


FIG. 39.—Separation of epiphysis, with chips of diaphysis.
FIG. 40.—Impaction of lower fragments into upper.

is not at all difficult to recognize clinically, and the bad results are not the fault of the diagnosis. The difficulty is with the proper reduction. We must bear in mind that we have two deformities to correct and to prevent—the posterior and the radial. We must also look for and if

FIG. 41.



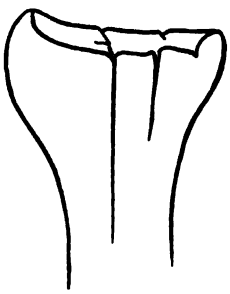
Lateral view. Anterior view.

Typical Colles' fracture.

necessary replace the ulnar fragment. Anæsthesia is usually necessary for proper reduction. Impaction, if present, must be broken up before reduction is attempted, and after the reduction and throughout the entire dressing we must bear in mind and prevent the tendency of the lower fragment to slip out of place. This tendency is most marked in

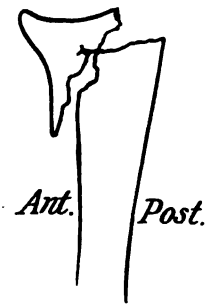
this variety of fractures. To prevent posterior displacement a pad should be placed over the dorsal surface of the lower fragment (extensor side of the wrist), and a second pad over the anterior surface of the lower end of the upper fragment. In addition, on the flexor surface of the forearm there should be a pad to fill in the anterior curvature of the radius. The dressing illustrated by Scudder is the simplest, and I should recommend it above all others. In fractures of the lower end of the radius with little deformity, and slight or no tendency to secondary displacement of fragments, there is no objection to the use of a light plaster-of-Paris dressing from the first; but in this variety, and all others with marked deformity and tendency to secondary displacements, a plaster-of-Paris dressing should be condemned. It is the most difficult dressing to apply and keep the fragments in position. When these pads are used it is unnecessary and dangerous to fix them with any great pressure. This variety of fracture should have constant

FIG. 42.



Stellate fracture.

FIG. 43.



Reversed Colles' fracture.

supervision. The proper reduction should be confirmed by the X-ray; it should be redressed in four or five days; massage should be begun at the latest on the tenth day; the dressing should be changed at the most once a week; and the patient should be instructed to move the fingers from the first. Good results depend, however, chiefly on reduction. No amount of pressure on pads or any form of dressing will correct the deformity; this must be corrected, usually under anæsthesia, at the first dressing. When the X-ray shows comminution of the lower fragment (Class 4), we cannot expect such good results. We must be most careful about proper reposition of the ulnar fragment, especially inversion. The usual very tight dressing is unnecessary. To prevent radial displacement the cross-traction method devised by Codman (see p. 99, Fig. 10) gives excellent results.

Class 9. (Fig. 42.) *Stellate Fracture of the Lower End of the Radius, with Longitudinal Fissures Extending into the Shaft.* Codman

has observed this six times, or 4 per cent. In three cases the ulnar styloid was broken. There is little deformity associated with this variety, no impaction, and no subluxation of the ulna. There is slight increase in the width of the wrist. Any simple dressing will do.

Class 10. (Fig. 43.) *Reversed Colles' Fracture.* This variety, first described by Roberts, of Philadelphia, has been observed five times by Codman (about 4 per cent.). In every case the ulnar styloid was fractured. The treatment is similar to that of a Colles' fracture, except the pads are changed to suit the different position of the fragments.

SURGERY OF JOINTS.

Traumatic Arthritis. In the contemplation of the possible injuries of a direct or indirect trauma to a joint there is much to be considered, and the frequent bad results of apparently at first slight injuries to the joint demonstrate that there is room for improvement both in the diagnosis and treatment. There are certain injuries to a joint which take place without fracture or dislocation, and which, if not recognized and treated, result in more or less permanent disability. The diagnosis of the majority of fractures near or into joints or a dislocation is not difficult, and the physician recognizing the injury at once resorts to proper treatment. In our discussion on fractures we urged the attention of the general practitioner to the great necessity of perfect reduction of the fragments in fractures near or into a joint, and the necessity of early massage and passive motion to prevent certain pathological changes in the joint which, if untreated, lead to more or less functional disability. After the reduction of a dislocation the treatment of the injury is by no means complete. We must bear in mind the rupture of the capsule or of one or more of the ligaments, and, in treating this associated injury, provide for that rest and fixation of the joint which will best insure permanent healing of the ruptured capsule or ligament. This fixation should always be associated with massage and passive motion.

It is those cases in which the trauma did not result in a positive fracture or dislocation that usually are neglected by the general practitioner. The injury is not recognized, and for this reason appropriate treatment is not instituted until the condition becomes chronic. In these injuries in the majority of cases a proper diagnosis and treatment in the recent state accomplishes perfect results. On the other hand, if the treatment is delayed it is always more difficult and frequently impossible to perfectly restore the function of the joint. The immediate effects of a direct or indirect trauma to the joint may be as follows: (*a*) An exudate with or without hemorrhage; this may take place into

the joint cavity alone (an effusion), or into the tissues without the synovial membrane; (*b*) rupture of the capsule of the joint; (*c*) rupture of one or more auxiliary ligaments; (*d*) complete or incomplete dislocation or tear of the intra-articular cartilage (as the semilunar of the knee-joint; (*e*) complete or incomplete separation of the articular cartilage; (*f*) slight incomplete fissured fractures of the articular ends of the bone; (*g*) tear-fractures of small bony prominences near the joint, with or without their dislocation between the joint surfaces. These subjects have been recently considered by Lauenstein,[1] van Hassel,[2] and von Hints.[3]

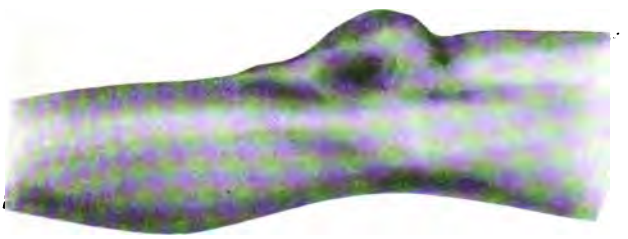
The clinical recognition of a traumatic joint exudate is not difficult in the exposed joints. It is most common and most excessive in the knee-joint. In the deeper joints, like the hip and the shoulder, the diagnosis by palpation alone is more difficult. In the hip we conclude that the capsule is distended with an exudate when the extremity assumes the position of flexion associated with slight abduction and outward rotation; and complete extension is impossible, even under anæsthesia. As a rule, palpation easily demonstrates the presence of an intrasynovial exudate. An excessive extrasynovial exudate may make the demonstration of the distinct joint effusion more difficult. This joint effusion may take place from a direct or an indirect trauma without any or only a slight laceration of the soft parts. Both Lauenstein and von Hints dwell upon the importance of removing the joint effusion by aspiration at once, and a second aspiration if it re-accumulates. If the joint effusion is not removed the capsule becomes distended, and this distention may be permanent and the cause of a chronic weakness of the joint, associated with a condition called chronic hydrops. This condition is difficult to treat satisfactorily in the later stages. I cannot agree with Lauenstein and van Hassel that this effusion should be removed by arthrotomy and irrigation of the joint when it occurs. In my experience, aspiration has always been sufficient, and there is but one indication to arthrotomy and irrigation in the recent state, that is an infection of the exudate. In the chronic case arthrotomy and irrigation should be performed when aspiration fails to prevent the recurrence of the exudate. As a rule, in joint injuries associated with effusion only aspiration followed by fixation of the joint in the most comfortable position will be sufficient. After three or five days massage and passive motion should be instituted, but the extremity should at least be fixed in a bandage for ten to fourteen days.

Rupture of the joint capsule or one or more of the joint auxiliary

[1] Centralblatt f. Chirurgie, 1901, vol. xxviii. p. 153.
[2] Journal de Chir. et ann. de la Soc. Belge de Chir., 1901, No. 6.
[3] Archiv f. klin. Chirurgie, 1901, Band lxiv. p. 980.

ligaments is very difficult to recognize clinically. An excessive effusion, especially when it is hemorrhagic, should make one very suspicious of a rupture of the capsule, or a ligament, or a fissured intra-articular fracture. After the effusion has disappeared the injured joint should be compared with its opposite, to ascertain if there is any increased joint mobility which could be only explained by a rupture of the ligament. Now and then on palpation a pit can be felt, due to the separation of the ends of the ruptured ligament. This clinical sign can frequently be demonstrated in partial or complete rupture of the quadriceps femoris tendon or the lateral ligaments of the knee-joint (Lauenstein).[1] Fig. 44 illustrates well the appearance about the knee-joint after the rupture of the quadriceps femoris tendon. I have recognized a partial rupture of this tendon on two occasions by palpation. In both the inner or medial half of the tendon was ruptured transversely just above the patella. The depression could be both seen and felt. A continuation of local joint pain when the patient again,

FIG. 44.



after the injury, begins to use the joint, associated with persistent joint weakness, even if one cannot make out increased joint mobility, should make one suspicious of a rupture of the capsule or one of the auxiliary ligaments. I quite frequently see patients treated for a so-called sprain of a joint who find, even after the second or third week, that they still have a local point of tenderness, which is increased by any attempt at using this joint. Perfect function is generally restored in these cases by fixation from one to five weeks, associated with massage and slight passive motion. Recently a man, aged seventy years, fell on the palm of the left hand with sufficient force to have produced the common Colles fracture. Directly after the injury there was no pain and no swelling, and but slight loss of function. The swelling began in about two hours. At this time I saw the patient. There was no deformity, except that due to effusion in the capsule of the joint about the lower end of the radius. The X-ray showed no fracture. In this case it was fully five weeks before the hand could be used without some support to

[1] Beiträge zur klin. Chirurgie, 1899, vol. xxiv. p. 673.

the wrist. Complete convalescence was almost as long as in an ordinary Colles' fracture. Although a rupture of one or more auxiliary ligaments could not be demonstrated, the clinical picture was sufficient to indicate the possibility. The patient was treated on this supposition. The forearm and wrist were fixed for four weeks, with daily massage and very slight passive motion. In some cases the complete rupture of one or more of the auxiliary ligaments can easily be demonstrated. If the ends are retracted a better result will be obtained by suture. In all cases of joint trauma the possibility of a ruptured ligament must be borne in mind. These cases should have some fixation of the joint, which not only supports but prevents excessive motion, for at least three to five weeks. The support should not be removed until pain and tenderness is absent on forced motions. Neglected, these cases usually result in a certain amount of permanent disability. Von Hints and van Hassel call attention to the large number of permanent disabilities following slight joint traumas not properly treated. The diagnosis and treatment of injuries to the intra-articular cartilages (the semilunar in the knee-joint), and separation of the articular cartilage with the formation of loose joint bodies have previously been discussed (PROGRESSIVE MEDICINE, December, 1899). A fissured fracture of the articular ends can usually be recognized by the X-ray shadow. The slightest displacement, if present, should be corrected. Tear fractures of small bony prominences near the joint, with their dislocation between the joint surfaces, is a difficult condition to recognize clinically. This fracture is usually associated with a dislocation of the joint, and the misplaced fragment may prevent reduction, which can only be accomplished by arthrotomy. It more rarely occurs without dislocation, and here the misplaced fragment interferes with joint motion. Eversman[1] reports two cases illustrating this point. The first patient, a boy, aged thirteen years, was seen eight days after the injury. He had fallen on the left hand, with the forearm in extension. He complained at once of pain and restricted motion at the elbow-joint. There may have been a dislocation to the outward, but if this was so, it had reduced itself. The elbow was swollen, and there was an area of ecchymosis over the internal epicondyle. One could not palpate the internal epicondyle. Flexion was possible only to 90°, extension to 110°, supination and pronation were not restricted. The ulnar nerve was paralyzed. This restricted joint motion could not be explained by the effusion. On more careful palpation it appeared as if the internal epicondyle was not present. The ulnar nerve had been caught between the humerus and olecranon. It was freed. The small bone fragment was replaced

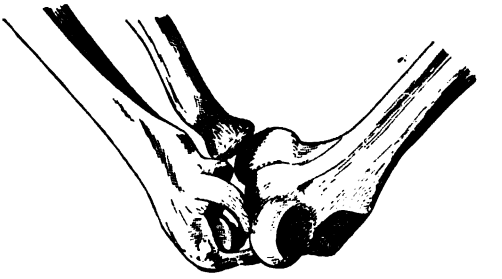
[1] Deutsche Zeitschrift f. Chirurgie, 1901, Band lx. p. 528.

and fixed by suture. Passive motion and massage were begun on the twelfth day. The ultimate result was a perfect one. Had the condition in this case not been recognized until much later we could not have expected the same good result. In the second patient, a boy, aged eleven years, the injury to the elbow was direct. For the first twenty-four hours there was little discomfort, and there was no dislocation. Within twenty-four hours the elbow had become swollen and painful. A diagnosis of contusion was made, although there was some restriction of motion. By the eighth day the joint swelling had almost disappeared, there was ecchymosis over the internal epicondyle, and this epicondyle could not be palpated. There was restriction of flexion and extension. Under ether, extension was not restricted, but flexion was. In this case the ulnar nerve was not injured. The fragment was removed.

In both cases we have a tear fracture, with a dislocation of a small fragment into the joint. Figs. 45 and 46 are anatomical preparations

FIG. 45.

FIG. 46.



illustrating the mechanism of this fracture. The internal epicondyle has been torn instead of the lateral ulna ligament (lig. collaterale ulnare). Careful examinations and the use of the X-ray will allow one, in the majority of instances, to recognize these various injuries just discussed, which may be associated with a joint trauma. If in doubt, the patient should be given the benefit of the treatment for the more serious condition. It can do no harm if it is not present. Prolonged fixation in plaster is bad surgery, although these injured joints need support; the dressing should be changed at frequent intervals to allow massage and careful passive motion.

The Relation of Trauma to Other Joint Diseases. Attention to this is made constantly in recent literature. We are called upon to recognize and treat not only the immediate results of the injury just discussed, but to be cognizant of the remote effects of the injury. Pyogenic infection of the injured joint or neighboring epiphysis is not

uncommon. The majority of cases of osteomyelitis in children give a history of trauma. Statistics show a very close relation between trauma and bone and joint tuberculosis. A trauma to a joint in a patient suffering with gonorrhœal urethritis is not infrequently followed by a gonorrhœal infection of the injured joint. Van Hassel[1] has called attention to the relation of trauma to a bone or joint in patients suffering from lues, and has recorded cases in which the slight trauma was followed by luetic periostitis, and, in some cases, the formation of a gumma. In individuals giving a history of previous attacks of articular rheumatism a slight trauma to a joint is very apt to be followed by an arthritis of a severe degree, which recovers much more slowly and is much more apt to become chronic than in other individuals. Experience so far demonstrates no relation between gouty arthritis and trauma, nor between rheumatoid arthritis (chronic arthritis deformans) and trauma. There should be no relation between a tabetic arthritis or one secondary to syringomyelia and an injury to the joint. But not infrequently a slight injury aggravates the pathological changes already present, and the patient and even the physician may at first, and in some cases for some time, attribute the joint condition to the trauma. The most difficult cases for diagnosis are the so-called *hysterical joints*. Here the patient complains of pain and weakness after even a slight joint injury. The symptoms are not relieved by treatment or time, and the physician naturally fears some grave pathological change. However carefully studied we find in a very neurotic patient a complaint of symptoms far out of proportion to the clinical signs about the joint. In such cases rest is the worst possible form of treatment. Nevertheless, one should be very careful in making a diagnosis of a neurotic joint. The diagnosis should be made by the most careful exclusion. A very interesting arthropathy, intermittent hydrops, has previously been discussed (see PROGRESSIVE MEDICINE, December, 1900).

Purulent Arthritis. I find little in the more recent literature of sufficient importance to add to that already previously discussed in PROGRESSIVE MEDICINE for December, 1899 and 1900. The great importance of recognizing early that the arthritis is due to some pyogenic bacteria is fully established, also the method of treatment: immediate arthrotomy, irrigation, and proper drainage. Gonorrhœal arthritis has been fully discussed.[2] Primary pyogenic arthritis is rare. It is usually secondary to a purulent focus in the diaphyseal side of the epiphyseal line. If there has been no external wound communicating with the joint, and we find in the joint effusion the staphylococcus pyogenes aureus, the streptococcus, or the pneumococcus, the probabilities are

[1] Loc. cit.

[2] PROGRESSIVE MEDICINE, 1900, p. 174.

that the joint infection is a secondary one, and, in addition to opening and irrigating the joint, we should look for the bone focus. In gonorrhœal infections, however, the opposite is the rule. Cases of gonococcus osteomyelitis are very rare, and so far it has been demonstrated that the bone infection was secondary. In typhoid fever, now and then, the typhoid bacillus has been found in the joint effusion. These cases have usually recovered after simple aspiration, and have been considered primary in the joint. I am inclined to the view that perhaps in many or in all of these cases the bone focus was overlooked, because we know that typhoid osteomyelitis is not an uncommon late sequela, and it has been clearly demonstrated that the typhoid bacillus may lie dormant in the bone marrow for a long time. Practically this form of purulent arthritis is not virulent, and usually recovers after conservative treatment with aspiration.

PURULENT ARTHRITIS DUE TO THE PNEUMOCOCCUS. Arthritis due to the pneumococcus as a complication or sequela of pneumonia is rare. Even sterile joint effusions during or after pneumonia are not common. The occurrence of joint pain or swelling during the acute attack or convalescence of pneumonia should make one very suspicious of a secondary infection of the joint. The fluid should be aspirated at once, and, if pyogenic cocci are present, arthrotomy and drainage should be performed. When this occurs in children the possibility of an osteomyelitis in the neighborhood of the involved joint should not be forgotten. In Perutz's[1] ten cases of pneumococcus osteomyelitis, eight were in children. Cole[2] reports two cases. The first patient was a colored man, aged fifty years. He was admitted to the hospital on the tenth day of an illness which consisted of fever, delirium, and cough. On examination there were physical signs of involvement of the apex of the right lung. Two days later the left ankle appeared swollen. On the tenth day the aspirated fluid was slightly purulent and blood-stained. The cover-slips and cultures demonstrated the presence of the pneumococcus. After arthrotomy and irrigation the patient's general condition improved. When he left the hospital the ankle was still swollen, but the wound had healed. During the illness a cardiac murmur developed, and there may have been an endocarditis. There is no question in this case that the arthritis was due to the pneumococcus, and this arthritis was probably secondary to the lung infection. Considering the age of the patient and the joint involved, an osteomyelitis may be excluded, although it is perfectly possible, yet uncommon, to relieve both bone and joint infection by arthrotomy. So that in this patient we cannot positively exclude osteomyelitis at the lower

[1] Reviewed in PROGRESSIVE MEDICINE, December, 1899, p. 224.
[2] Johns Hopkins Hospital Bulletin, June, 1902, vol. xiii. p. 143.

end of the tibia. In the surgical clinic of the Johns Hopkins Hospital arthrotomy and irrigation of the elbow-joint and knee-joint were performed on a girl, aged thirteen years, for purulent arthritis in which streptococci were found. The patient left the hospital apparently well, but returned three months later with swelling, pain, and tenderness over the head of the tibia and upper end of the ulna. In each position I found at the operation a purulent focus in the bone. This is a good illustration that the primary focus in the bone may be overlooked. Pneumococcus arthritis may occur independently of acute lobar pneumonia. This is even more rare. Cole's second case belongs to this group. The patient, a colored man, aged fifty-five years, was admitted to the hospital complaining of pain in many joints. Both knee-joints had been swollen for five weeks. Three days before admission he had had a chill, and was delirious when admitted. The clinical picture was one of general infection with involvement of both knee-joints and ankle-joints. The mental condition and marked stiffness of the neck suggested cerebro-spinal meningitis. Cultures from the blood, the joint fluid, and the spinal canal contained the pneumococcus. In the note on the autopsy nothing is stated in regard to the examination of the bones. This case, however, belongs to a group of little interest to the surgeon, as it represents a general pneumococcus septicæmia in which the joints were involved in the general process. At the autopsy it was demonstrated that the patient had chronic arthritis deformans, and from the family of the patient Cole was able to ascertain that the man had for several years suffered frequently with pain and swelling in many joints. The cases in the literature demonstrate that any chronic arthritis is more likely to become infected than the normal joint.

Herrick,[1] of Chicago, gives us an excellent résumé of this subject, with the entire literature, and the details of the fifty-two reported cases. Cave,[2] in 1891, collected thirty-one cases, and Herrick has been able to add twenty-one cases, including three of his own, but not including Cole's two cases. Herrick does not mention the possibility of osteomyelitis, and does not give any reference to those cases which have been reported in the literature, but records only four cases under twenty years of age. The possibility of osteomyelitis in these four cases, and even in some of the adult cases, cannot be excluded. The mortality has been high, over 65 per cent. Death, however, cannot be attributed to the joint complication. The arthritis, undoubtedly, indicates a general infection. Nevertheless, early recognition with incision and drainage of the joint cavity should give the patient a better chance for recovery.

[1] American Journal of the Medical Sciences, July, 1902, vol. cxxiv. p. 12.
[2] Lancet, January 12, 1901

In some cases in which the patients are not very ill, and in which the joint signs are not very severe, aspiration of the fluid may be tried first. In two of Herrick's cases—an elbow, and a hip and knee—both patients recovered from the pneumonia. The elbow-joint and the knee-joint effusions were relieved by simple aspiration, and there was no resultant ankylosis. On the other hand, the arthritis of the hip, which was not treated, resulted in ankylosis. A case reported by Raw, an arthritis of the right knee, recovered after aspiration. In Nicolaysen's patient, a child, aged three weeks, the arthritis of the right elbow recovered without operation. These cases also demonstrate that trauma and previous disease of the joint increases the probability of the localization of the infection; 61.5 per cent. had been confined to a single joint, usually a large joint. The knee is the most common joint.

Allen, and Lull,[1] of Cleveland (included in Herrick's report, Case 47), report a case of pneumococcus arthritis not secondary to pneumonia. It differed, however, from Cole's second case, in that a single joint, the knee, was involved. The patient was a female, aged forty years. For three days she had suffered from pain in the abdomen, and for two days pain in the left knee-joint. The patient had not appeared very ill. There were general symptoms of infection: fever and a leucocytosis of 27,000. The left knee was distended with an effusion which was aspirated at once. The fluid was thick, yellowish pus. On account of the character of the effusions the knee-joint was at once opened by two incisions, irrigated, and drained with gauze. Forty-eight hours later the general condition of the patient was so critical that the limb was amputated in the middle third of the thigh. Death took place on the tenth day after the amputation. The general symptoms of infection remained about the same. The amputated stump had suppurated. The autopsy demonstrated an infected stump containing the pneumococcus and the staphylococcus pyogenes aureus, the internal organs the pathological changes of a general infection. There is no note on the condition of the bone. Blood cultures before death were sterile. This case of Dr. Allen represents an unusually virulent type.

The surgical indications for the treatment of joint complications following pneumonia are pretty clear. We must remember that arthralgiæ, with and without effusion, are more common than septic arthritis due to the pneumococcus or other pyogenic bacteria. Pain in the joint without swelling should be carefully watched. On the first appearance of the effusion it should be aspirated, and the fluid studied bacteriologically. If the local signs are mild we can delay; if they

[1] Annals of Surgery, 1901, vol. xxxiv. p. 526.

are severe, or if the milder case is not relieved by aspiration, the joint capsule should be incised freely, and the cavity washed out, first with 1 : 1000 bichloride solution, and then with boiled water or salt solution.

The incision should be drained by a strip of protective; gauze or a rubber drainage-tube cause too much insult to the already inflamed synovial membrane. The irrigation should be continued daily until the local signs distinctly indicate that the local infection is subsiding. Generally one or two irrigations, if properly performed, are sufficient. When it is evident that the inflammation has not been subdued, or is distinctly progressing, a second operation should be performed at once; more incisions should be made, opening every pocket of the joint capsule; there should be search made for periarticular abscesses, and in some cases, especially in children, the neighboring bone end should be explored for a purulent bone focus. Pneumococcus arthritis seldom demands this second operation, especially if the first is performed early and properly. In consideration of the pneumonia the arthrotomy should be done under local cocaine anæsthesia. With this anæsthesia it is perfectly possible to open, irrigate, and drain any joint, even the hip. If the second and more radical operation becomes necessary, general anæsthesia must be used in the majority of cases. These recent articles on pneumococcus arthritis neglect to call attention to the possibility of simultaneous osteomyelitis, especially in children. In reading the individual cases more carefully, one feels that it is just to criticise the physician for the frequent delay of the exploratory aspiration and the transfer to the surgeon for arthrotomy and irrigation. One familiar with the pathology of pyogenic arthritis knows that the pathological changes in the synovial membrane and surrounding soft parts are extremely rapid, and that these changes must be checked in their early stage if we wish to preserve normal joint function. We know that the rapidity of these pathological changes vary with different pyogenic bacteria, most rapid with the staphylococcus pyogenes aureus, the streptococcus somewhat less, the pneumococcus and the gonococcus least. Yet the difference is so slight that there is no justification for delay in proper treatment in any of these infections. The rare typhoid synovitis stands alone in that the condition so far has been relieved by simple aspiration. Now and then cases of pneumococcus and gonococcus synovitis have been relieved by simple aspiration when this is performed in the very early stages.

Gonorrhœal Arthritis. Recent literature seems to show that the physician is not always familiar with the excellent results of the surgical treatment of gonorrhœal arthritis. Markheim,[1] in reporting fifty-

[1] Deutsche Archiv f. klin. Med., 1902, lxxii. p. 186.

two cases observed during the last seven years in Eichhorst's clinic, concludes that his results had been particularly good, which he attributes to the abstention from surgical intervention. In only one case was surgical treatment resorted to. Yet the so-called good results of Markheim were as follows: Of the fifty-two cases only thirteen were discharged well; complete ankylosis followed in five cases, partial ankylosis in seven. In the other patients when they left the hospital the affected joint was still swollen and slightly tender. In only one case were cultures taken from the joint. Even without the bacteriological proof, these results should be considered very bad. William S. Thayer,[1] in reviewing this article, writes that he cannot concur with Markheim's conclusion, and remarks that "modern experience has emphasized the importance of aspiration, bacteriological examination of the joint fluid, and surgical operation in many cases. Early surgical treatment in joints from which gonococci or pyogenic cocci are obtained on culture will probably save many joints." In looking over the cases of gonorrhœal arthritis in the Johns Hopkins Hospital clinic, the results of treatment have established a cure in every case in which we were able to institute treatment before the gonorrhœal infection had destroyed the capsule or articular cartilages of the joint. In sixteen out of forty cases arthrotomy and irrigation of the joint was performed because we found on aspiration the gonococcus. In every case it was demonstrated in cover-slips, in six cases it was cultivated. The result of the arthrotomy and irrigation was an almost immediate improvement. When the aspirated fluid has been free from micro-organisms we have not resorted to arthrotomy, and these have recovered with good function of the joint.

We have had to excise one hip-joint and one knee-joint, because when the patient was admitted to the hospital the disease had extended to the bone ends, and we observed the rare condition of gonorrhœal osteomyelitis.

In the differential diagnosis of joint lesions we must remember that gonorrhœal arthritis frequently begins as a polyarticular lesion—in our cases 60 per cent.—although when the patients were admitted to the hospital more than one joint was affected in only 11 per cent. of the cases. This point is frequently overlooked in the anamnesis. Markheim's observations agree with mine. In his cases 56 per cent. were polyarticular. Fortunately, however, usually only one, less commonly two, and very rarely more joints progress to that acute stage which demands operative interference. The indication for arthrotomy in the acute stage is the presence of the gonococcus in the exudate.

[1] American Journal of the Medical Sciences, August, 1902, vol. cxxiv. p. 346.

Gonorrhœal Arthritis of the Hip. It seems to be the popular opinion that the hip-joint is rarely involved in gonorrhœal joint infection. I have observed it three times in about fifty cases, 6 per cent. In my own experience the order of frequency of involvement is about as follows: knee, ankle, wrist, elbow, shoulder, and hip. Markheim[1] mentions the hip next to the knee. König[2] writes that he has observed during the past five years eighteen cases of severe gonorrhœal arthritis of the hip. One died from double pyelitis; in only six cases was the perfect function of the joint restored; in four cases there was permanent shortening; in the other cases more or less limitation of motion. I have previously discussed the diagnosis and treatment of this form of arthritis in detail.[3] These observations should impress one with the importance of considering gonorrhœa as an etiological factor in case of arthritis of the hip.

General Infection in Gonorrhœa. Ward[4] advances the view that there are two forms of general infection: one due to the toxin, and the other due to the metastatic gonococcus itself. This view might explain the monoarthritides or polyarthritides, in which, so far, we have been unable to demonstrate the gonococcus in the tissues or in the effusion. Ward emphasizes a very important point in the treatment of the acute local infection—that is, it should be free from instrumental, mechanical, and chemical violence. This local traumatism increases the danger of general infection. All authorities agree on this point. In both men and women the local gonorrhœal infection in its early and acute stage should be handled with the greatest care. But, on the other hand, these patients should have local treatment until the infection is absolutely cured. Ullmann[5] reports five cases of general infection following gonorrhœa, observed during six months in the medical clinic of Greifswald. In four cases the general infection started from a small prostatic abscess, in two the prostatic abscess was not suspected, and was only found at autopsy. In the fifth case the general infection was associated with urethritis. All the patients died. Ullmann emphasizes the importance of the most careful examination of the prostate in cases of obscure general infection in men.

Latent Gonorrhœa. There is sufficient observation to demonstrate that the gonococcus may remain dormant for considerable periods, and then give rise to a very acute joint infection. The stimulus to this is usually a traumatism. We quite frequently observe gonorrhœal bubo in men long after the urethritis has apparently been cured. The inguinal

[1] Loc. cit. [2] Berliner klin. Wochenschrift, November 19, 1900, p. 1078.
[3] Progressive Medicine, December, 1900, p. 182.
[4] British Medical Journal, March 30, 1901.
[5] Deutsche Archiv f. klin. Med., 1901, lxix. p. 309.

adenitis first manifests itself after some trauma or strain. Niebergall[1] reports four cases in which he considers that a latent gonorrhœal infection was reignited by a trauma. In all of his cases the acute gonorrhœal infection followed the dilatation and curettement of the uterus. We not infrequently observe arthritis following traumatism, which can only be explained by latent gonorrhœa.

Gonorrhœal Myositis. A purulent myositis due to the gonococcus, not secondary to an arthritis, is a very rare observation. Ware,[2] of New York, reports a case confirmed by careful bacteriological and histological study. This patient had gonorrhœa two months previous to the onset of the myositis, and in the fourth week a slight arthritis in the left knee, which recovered. The myositis was confined to the muscles forming the posterior axillary fold. Here Ware found on palpation an area of induration about the size of a walnut. Observed a few days, the area increased in size, also the local pain and tenderness. On incision under local anæsthesia there was no pus, but the muscle was œdematous, grayish in color, and friable. The wound was left open. There was immediate relief from pain, and in about six weeks the wound had healed and the area of induration had almost disappeared. This appears to be the first case of gonorrhœal myositis in which the diagnosis was confirmed by bacteriological and histological proof. In the literature there are only three cases in which this diagnosis was made, but in all it was based upon the clinical picture only: Rona,[3] two cases, both in the quadriceps femoris; here the area of induration disappeared without operation; Eichhorst,[4] one case. The area of induration in this case was also confined to the quadriceps femoris, and recovered without operation. König and others are inclined to the view that many of the cases of so-called chronic muscular rheumatism rest on a basis of gonorrhœal infection.

The Joint Lesions of Acute Rheumatism. Recent literature has added nothing to lessen our ignorance on the etiology of rheumatism. Stern's[5] article, just received, on the pathogenesis of acute articular rheumatism adds nothing to the monograph of Pribram,[6] previously reviewed. The diagnosis of the joint lesions of acute rheumatism is seldom difficult, and for this arthritis there is no necessity for surgical intervention, except now and then an aspiration of an effusion of high degree. However, as the symptom-complex of acute articular rheu-

[1] Hegar's Beiträge zur Geburtshülfe und Gynäkologie, Bd. ii., H. 1.
[2] American Journal of the Medical Sciences, 1901, vol. cxxii. p. 40.
[3] Archiv f. Dermatologie und Syphilis, 1892, p. 250.
[4] Deutsche med. Wochenschrift, 1899, p. 685.
[5] Medical News, August 23, 1902, p. 340.
[6] PROGRESSIVE MEDICINE, December, 1900, p. 185.

matism may be closely simulated by other diseases with joint lesions which demand early surgical intervention, we must be on the alert. In rheumatism we have no evidence that the joint lesions are ever produced by pyogenic bacteria, but a secondary infection with these bacteria of an acute rheumatic joint is quite possible. The diagnosis can be made by the bacteriological study of the aspirated fluid. The demonstration of pyogenic bacteria should at once be followed by arthrotomy and irrigation. Fortunately, this secondary infection is rare. Acute gonorrhœal polyarthritis very closely resembles rheumatism, and without much doubt this form of arthritis is most frequently incorrectly diagnosed rheumatic. The presence of a local gonorrhœal infection should make one suspicious. The demonstration of gonococci in the effusion would be positive. The treatment has been discussed. Polyarthritis purulenta secondary to puerperal infection, or any other local infection becoming general, usually gives a picture of more profound general sepsis than rheumatism. Bacteriological examination of the effusion will make the diagnosis. Unfortunately, when many joints are infected with these purulent bacteria there is little hope from surgical intervention. The polyarthritis observed now and then, during or after the various acute infectious diseases, might now and then be confused with an attack of acute articular rheumatism. In many of these cases the effusion is sterile, in which instance conservative treatment should be followed. Now and then pyogenic bacteria are found, and in this case the treatment should be the same as in any case of septic arthritis. As already stated, if the typhoid bacillus is found aspiration is sufficient. In cerebro-spinal meningitis the specific coccus of this disease is now and then found in the joint effusion (Osler[1]) as well as in the cerebro-spinal fluid. In view of the fatality of this disease, aspiration should be tried at first. The organism is apparently of low virulence as far as the joint infection is concerned. The most important differential diagnosis is that from multiple epiphysitis in children, in which the signs of the bone focus are usually referred to the joint. Early incision of the pus focus in the end of the bone is very important. In gout many joints are seldom involved in the acute attack, and the differential diagnosis is of less importance. This differential diagnosis in acute rheumatism has recently been considered by Weber.[2]

THE CLINICAL PICTURE OF THE ARTHRITIS IN ACUTE RHEUMATISM. Unfortunately, there is nothing in the appearance of the acutely swollen and painful joint in rheumatism to differentiate it from other forms of acute arthritis. The diagnosis of rheumatism is based upon the symptom-

[1] Arthritis of Cerebro-spinal Fever. Boston Medical and Surgical Journal, December 29, 1889.

[2] Medical News, August 23, 1902, p. 339.

complex of this disease and its relation to the involvement of many joints. In acute rheumatism one joint is seldom involved alone. It is the polyarthritis that characterizes the disease; also, the non-uniformity of the extent of the arthritis. One or more joints may be only painful, a few show only slight effusion. A very severe arthritis may be present in none or only one or two joints. Differing from other forms of acute polyarthritis, small joints are not infrequently involved in rheumatism. The clinical picture of a single joint in rheumatism showing an arthritis of extreme degree does not differ from that seen in any other form of acute arthritis. It is this fact that makes the diagnosis so difficult when one sees the patient toward the end of the attack, when the other involved joints have recovered. We cannot differentiate this picture from an arthritis due to secondary infection of pyogenic cocci, except by aspiration and bacteriological study of the effusion. This procedure is the most important point in the treatment of a severe arthritis of the rheumatic attack, a point so frequently neglected. The most interesting and remarkable instance is the rapid and perfect recovery of the joint after an attack of acute rheumatic arthritis. We see this joint intensely swollen, due to the intrasynovial and extrasynovial exudate, the skin over, above, and below the joint may be œdematous; there may be areas of induration due to the organization of the exudate, areas of subcutaneous ecchymosis are common; there is intense muscle spasm, no joint motion is allowed; the skin may look as red as the skin over a purulent arthritis or an abscess. Yet if this arthritis is due to the specific toxin of rheumatism perfect resolution may take place. The recovery is frequently rapid. It is just this clinical picture that so frequently puts the general practitioner off his guard and influences him to make a diagnosis of rheumatic arthritis. If he is correct no harm is done. On the other hand, if this arthritis is due to some pyogenic organism, and it is allowed to go to this advanced stage, the joint is hopelessly damaged, and recovery with ankylosis can only be expected. The diagnosis of rheumatism in a case of arthritis of the degree just described should be made after the most careful and positive exclusion of pyogenic infection. Unfortunately, our surgical records show that rheumatic arthritis of this degree, a rare disease in this country, is the most common diagnosis, and the more common disease, purulent and gonorrhœal arthritis, and arthritis secondary to epiphyseal osteomyelitis, usually go unrecognized to that stage of the disease in which operative intervention cannot restore the function of the joint. The pathology of acute arthritis has been previously described.[1]

[1] PROGRESSIVE MEDICINE, December, 1900, p. 171.

THE JOINT LESIONS OF CHRONIC RHEUMATISM. According to Osler, a chronic arthritis as a sequence of acute rheumatism is extremely rare. The disease may be confined to a single joint, but, as a rule, many joints are involved. The symptoms are intermittent attacks of pain, slight stiffness, rarely a little swelling. These symptoms are aggravated by exposure to cold, dampness, and changes in the weather. The diagnosis of chronic rheumatic arthritis is a very dangerous one, especially when a single joint is involved. Especially is this so in children. The disease must always be differentiated from tuberculosis. This has recently been discussed by Taylor,[1] who writes that chronic joint disease in children in nine cases out of ten is tuberculosis. Taylor dwells upon the importance of an early correct diagnosis and treatment, and the pathetic results of delay.

The Joint Lesions of Gout. Futcher,[2] in his recent paper before the American Medical Association, based on the study of 32 cases of definite gout among 14,000 patients admitted during the twelve years of the medical clinic of the Johns Hopkins Hospital, has established the fact that gout is not as rare in this country as previously supposed. The arthritis in gout seldom comes to the surgeon for operative treatment. Nevertheless, in the differential diagnosis of arthritis gout must always be borne in mind as a possible etiological factor. The acute arthritis in gout is most frequently incorrectly diagnosed rheumatism (Futcher[3]). The most important point in the diagnosis of gout is the demonstration of the existence of tophi. In 16 out of Futcher's 32 cases the diagnosis was confirmed by this finding. The second most important fact in the diagnosis is the involvement of the toe-joints in the beginning of the attack. Nothing is yet established to indicate that surgical intervention is of any value in the treatment of gouty arthritis.

The surgeons are now and then called upon to excise bursæ, which are filled with tophi, or excise joints more or less destroyed by the deposits of biurate of sodium. The most common joint to show this advanced stage is the metatarso-phalangeal joint of the great toe. The deformity and discomfort are completely relieved by excision. I have had three cases. This destruction producing ankylosis is, fortunately, seldom observed in the larger joints. The tophi when they form about large joints are usually periarticular, in the bursa or outside the synovial sack. Excision always gives relief, but we have no observations that this operative interference gives immunity to the tissues about the joint from further attacks. The most interesting recent contribution to the

[1] Chronic Joint Diseases in Children. Medical News, August 16, 1902.
[2] Editorial, Journal of American Medical Association, July 19, 1902, p. 139.
[3] Johns Hopkins Hospital Bulletin, May, 1902, vol. xiii. p. 116.

anatomy of gout is by Bennecke.[1] He carefully describes the histological picture about the deposits of the uric-acid salt crystals, and confirms the observations of Ebstein that these deposits are always in the necrotic tissue and never in the living. The destruction of the joint in gout is due to the deposits of the crystals beneath the articular cartilage. After this has taken place and the cartilage has separated there is little hope of restoring joint function. An excision of the joint is indicated. So far I have never observed this except in the metatarsophalangeal joint of the great toe.

Arthritis Deformans. This chronic disease, which is frequently incorrectly called rheumatic gout or rheumatoid arthritis, generally affects more than one joint. As a polyarthritis in adults it is not difficult to diagnose in its later stages. The smaller joints are usually first involved, then the larger joints. During the progress of the disease there may be acute exacerbations in which the diagnosis of acute articular rheumatism is often incorrectly made. As the disease progresses the joints become ankylosed in deformed positions, due to the destruction of bone and cartilage. Recent authorities are inclined to place this form of arthritis among the arthropathies of spinal cord origin similar to the arthropathies in tabes and syringomyelia. Latham[2] has recently contributed an article in support of this view. Preble and Hektoen,[3] in a very carefully studied case of multiple fibromata of the nerves associated with arthritis deformans, demonstrated lesions of the spinal cord. The nervous etiology of this form of arthritis, however, is not yet fully established. It, however, apparently has no relation to the specific diseases rheumatism and gout. Until the etiology is established the practical point for the general practitioner is to recognize this disease in its earlier stages, before destruction of the cartilage and bone have hopelessly impaired the function of the joint. Perhaps in this stage something might be done, at least, to arrest the disease. In the later stages of ankylosis with deformity something can be expected from surgical intervention. The scanty literature on this subject has been presented recently by Tinker,[4] and here it is clearly shown that resection of the joint relieves the deformity and gives the patient a much more useful limb. Of course, the operation has no effect upon the course of the disease, but in properly selected cases the operation unquestionably adds to the comfort of the patient and to his power of getting about. König has resected the hip in four instances. Poppert and Müller report two cases of resection of the hip, two of the

[1] Archiv f. klin. Chirurgie, Band 1902, lxvi. p. 658.
[2] Lancet, 1901, vol. clx. p. 998.
[3] American Journal of the Medical Sciences, January, 1901, vol. cxxi. p. 1.
[4] American Medicine, January 18, 1902, p. 122.

knee, and three of the wrist, with favorable results. I have resected one hip with a very satisfactory result. The patient now can walk without crutches. Collison reports two good results after resection of the elbow. I believe that the pathetic condition of many of these patients could at least be temporarily improved, perhaps for a number of years, by resection.

CHRONIC ARTHRITIS DEFORMANS IN CHILDREN. As stated before, most forms of chronic arthritis in children are due to the tubercle bacilli. A chronic form resembling the chronic arthritis of adults is not uncommonly observed. Apparently, it is very rare in this country. The disease in children, according to recent authorities, has a different etiology from that in adults. My attention was first called to this by a case of polyarthritis deformans in a girl, aged ten years, observed in the Johns Hopkins Hospital surgical clinic. Tuberculosis was excluded by the absence of tuberculin reaction and the negative animal inoculations and histological studies of pieces of tissues removed from the involved joints. The disease in children differs from that in adults in the fact that the synovial membrane and the soft parts of the joint are chiefly involved in the chronic inflammatory process, and there is, as a rule, little destruction of cartilage and bone which is characteristic of the disease in the adult. Pathologically the picture of the two diseases is different. Schüller,[1] in a very exhaustive article, is very emphatic that this disease must be differentiated from arthritis deformans. He calls attention to the clinical resemblance, but the different pathological anatomy. Schüller advocates the name polyarthritis chronica villosa, because the inflammation is situated in the synovial membrane and its villi. He describes two forms: the hyperplastic (polyarthritis villosa hyperplastica), in which the swelling of the joint is not due to an effusion, but to an hypertrophy of the synovial membrane and its villi. The second form is characterized by the atrophy of the synovial membrane and its replacement by fibrous tissue, producing ankylosis (polyarthritis villosa ankylopœtica). Schüller has demonstrated in his cases the presence of a bacillus and a coccus. According to his observation the disease is more common in children, but has been observed in adults. Schüller's bacteriological findings have not yet been confirmed. The most interesting article on this form of polyarthritis in children appeared some years ago by a Russian, Tschermak.[2] The disease seems to be quite common in Russia. Tschermak finds forty-nine cases recorded in the literature. In a number of cases the arthritis began as an acute infection. In the majority, however, it was of a subacute or chronic nature from the beginning. The arthritis most

[1] Berliner klin. Wochenschrift, 1900, Nos, 5, 6, 7, and 32.

[2] Wratsch, 1898. Reviewed in Centralblatt f. Chirurgie, 1898, No. 3, p. 853.

frequently follows some illness of a depressing character. It begins, as a rule, with the small joints, and later involves the larger joints. The disease is progressive and apparently incurable.

The Joint Lesions in Hæmophilia. If a surgeon of König's knowledge of and experience with joint affections makes a diagnosis of tubercular arthritis of the knee on two occasions, and experiences at the resection of the joint almost fatal results from hemorrhage, because the arthritis was a joint lesion of hæmophilia, and not tuberculosis, then contributions to the diagnosis of bleeders' joints are of special practical importance. The disease must be a very rare one in this country. We have never observed a joint lesion due to hæmophilia in the Johns Hopkins Hospital clinic, although we have had a few cases of the disease. According to Osler, the arthritis may be the first symptom of the onset of a hemorrhage from some other part of the body. The literature on the subject is very meagre. The earliest important contribution was made by König in 1892. Mermingas,[1] in reporting three cases, observed recently in König's clinic, in Berlin, gives a short résumé of the ten important contributions to the literature. If one will take a very careful history, cases of hæmophilia, with or without joint complications, will seldom be overlooked, and the surgeon taking this precaution will rarely operate upon a hæmophilic patient in ignorance of the disease. The history of previous slight attacks of joint pain and swelling should make one especially vigorous in his investigation into other possible evidences of this bleeding tendency. These patients, as a rule, give a history of epistaxis, unusually copious bleeding from small cuts, large areas of ecchymosis, or even hæmatoma from slight contusions. It is interesting and important to note that these patients do not always bleed after extraction of teeth, nor always after a cut. According to Grandidier,[2] epistaxis is the most important previous symptom (169 out of 334 cases of hæmophilia). D. Hayes Agnew[3] observed that in some hæmophilic individuals bleeding only took place when they were injured in certain parts of the body. Mermingas'[4] contribution is of additional interest, because of the Roentgen picture of the hæmophilic joint. Mermingas summarizes the clinical picture of this form of arthritis illustrated by his three cases and others in the literature somewhat as follows: Usually there is a previous history of epistaxis or some other hemorrhage. The arthritis may or may not be secondary to a trauma, usually slight. The joint symptoms at first are slight, and consist of pain, slight swelling, and a little impairment of function. These symptoms soon disappear; then there is recurrence of the symptoms in this or other joints. Now and then

[1] Archiv f. Chirurgie, 1902, Band lxviii. p. 188.
[2] Quoted by Osler in his Text-book. [3] Ibid. [4] Loc. cit.

only one joint is involved in the recurrent attacks. Usually after a number of attacks in one joint, very rarely after a single severe attack, the arthritis becomes permanent and chronic, and ankylosis with contraction may take place. The pathological picture demonstrates that the first change is hemorrhage intrasynovially and extrasynovially; later inflammatory changes in the capsule, resulting in fibrous tissue. Not uncommonly the destructive inflammation may extend to the cartilage and bone ends. In some instances first observed by König in the knee-joint the entire joint may be disorganized. Bearing these facts in mind, the diagnosis is not difficult. It does not seem to be dangerous to aspirate the joint effusion for diagnosis After this aspiration, recent experience has demonstrated that it is best to inject a sterile solution of gelatin (Krause[1]). Krause's patient was a fifteen-year-old hereditary hæmophile, who suffered with frequent swellings of the joints. On admission to the clinic the effusion to the left knee was aspirated. It consisted of almost pure blood. Twenty-four hours later, when the bandage was removed, blood squirted in a stream from the punctured wound; 200 c.c. of a 1 per cent. gelatin salt solution were at once injected into the joint. The hemorrhage ceased. Intrasynovial and subcutaneous gelatin injections were repeated at intervals, five times, with relief of the joint effusion. No hemorrhage took place from the punctured wound after the gelatin injections. This experience should influence us to follow an exploratory aspiration of a hæmophilic joint by gelatin injection. The only treatment, therefore, that we have to check the hemorrhage into the joint is gelatin injection. In addition, during the acute attack the joint should be kept at rest and snugly bandaged. If there is slight ankylosis and contraction one should never attempt forcible correction. The contraction should be overcome by gradual extension, which will give good results in the early stage of the disease, as recorded by Mermingas. Operative interference to correct a deformity is contraindicated. In the further treatment of the disease the patient should be cautioned against trauma, the affected joint or joints should be protected by a bandage, and in some cases a temporary supporting and protective apparatus should be applied.

Hemorrhagic Arthritis. Blood in the joint effusion properly interpreted has diagnostic significance. After a contusion of the joint one will always find a slightly blood-stained effusion. When the fluid is almost pure blood it indicates a rupture of the capsule or an intra-articular fracture. If the injury is a very slight one and the effusion very sanguineous, one should suspect hæmophilia. In the joint lesions of scurvy and purpura the effusion is generally hemorrhagic. In tuber-

[1] Referred to by Sackur, Mittheilungen aus den Grenzgebieten der Medicin und Chirurgie, 1901, Band viii. p. 188.

culosis one rarely finds blood except after a trauma. In a chronic joint lesion a hemorrhagic effusion is very suggestive of a new-growth. We rarely observe even microscopic evidence of blood in the effusions of chronic arthritis of all the varieties just discussed.

The Joint Lesions of Syphilis. Before the discovery of the tubercle bacilli the diagnoses luetic arthritis and osteomyelitis were very common, and in the older literature we see numerous articles on the bone and joint lesions of syphilis, in recent literature, very little, and I am inclined to feel that quite frequently this very important etiological possibility is overlooked both by the general practitioner and the surgeon. The great importance rests upon the fact that in its early stages the arthritis is immediately relieved by antisyphilitic treatment. In the later stages of gumma formation a combination of medicinal and conservative operative intervention usually saves the joint with good function. The acute arthritis of lues is most frequently diagnosed rheumatism; the chronic arthritis, tuberculosis. Borchard,[1] in reporting a very interesting case of chronic arthritis of the knee with gumma formation, gives a very careful résumé of the literature. We must recognize first clinically the acute arthritis of the so-called secondary stage of lues. It is characterized by pain and effusion in one or more of the larger joints; not infrequently only one joint is involved. As a rule, one or both knees are the most usual site of the arthritis. The joint symptoms appear simultaneously with a skin eruption. The fluid is clear, of a lemon-yellow color and viscid consistency. The synovial membrane is slightly injected. Properly treated, the arthritis disappears with the same rapidity as the other secondary lesions. De Grandmaison and Boidin,[2] in reporting a case of acute hydrarthrosis of the left knee occurring simultaneously with the other secondary syphilitic lesions, write that they find very few similar cases recorded in the literature. It is, however, the joint lesions of the later stages of syphilis that are more difficult to recognize. The arthritis occurs in two forms: a primary infection of the synovial membrane, and a secondary arthritis from an osteomyelitis of the epiphysis, or a periostitis. The primary chronic luetic arthritis is very difficult to recognize clinically. The history of a luetic infection is suggestive, but, of course, not positive. It resembles closely primary tubercular synovitis. Only one joint may be involved, as in tuberculosis. The onset of the disease is rarely acute. The joint is painful and gradually swells. The absence of the tuberculin reaction, not mentioned by Borchard, would be a great help in the diagnosis. The correct diagnosis can usually be made by arthrotomy. The appearance of the syphilitic synovitis in its later stage should be

[1] Deutsche Zeitschrift f. Chirurgie, 1901, Band lxi. p. 110.
[2] Archives Générales de Méd., 1902, p. 58.

recognized. The hypertrophy of the synovial membrane and its villi are present in both diseases, but in syphilis we will find one or more distinct gummata situated in the synovial sac. The tubercle of tuberculosis is seldom as large as the gumma. In the early stage, however, a small gumma, not infrequently multiple, would be very difficult to distinguish from a tubercle. In tuberculosis the destruction of the cartilage takes place at the border, and is usually quite extensive. In lues the central portion of the cartilage is first affected, and the destruction of much less extent. This form of synovitis in both diseases should be treated by arthrotomy and irrigation, and never, even in tuberculosis, by a resection. The absence of the tuberculin reaction and the histological study of a piece of the synovial membrane, combined with the negative animal inoculation, should exclude tuberculosis. These findings should indicate antisyphilitic treatment and give a better prognosis. If one or more large gummata are present the diagnosis is usually made without any difficulty. The gumma should be excised and the wound in the joint closed after irrigation. Borchard's case was of this character, and the result a most satisfactory one. We must remember that there is a form of tubercular synovitis in which we find a solitary large circumscribed tubercle. They may reach the size of an egg. The tubercle is generally flattened and may be pedunculated. The pedunculated tubercle may simulate a loose joint body. This large tubercle can be distinguished from the gumma. The gumma is of firm consistency, it is never caseated, although there may be a central area of coagulation necrosis. The tubercle is seen in two forms: one, a tumor of jelly-like consistency and grayish-red color, surrounding which we generally see a few miliary tubercles; in the other form the tubercle is caseated.[1] Borchard does not mention this form of tuberculosis, but calls attention to the fact that luetic gumma may become pedunculated and form soft joint bodies. The primary luetic arthritis, which is single or multiple gumma formation in the synovial membrane, rarely produces disorganization of the cartilage and bone ends of the joint. It rarely suppurates, but if not recognized and properly treated in the early stages it produces ankylosis of the joint by the resultant scar formation in the healing of the gumma. The arthritis secondary to luetic periostitis and osteomyelitis is recognized by the bone lesion, and will be discussed later on.

THE JOINT LESIONS OF CONGENITAL SYPHILIS. Borchard[2] also discusses these lesions. The same two forms, primary and secondary arthritis, are to be recognized. In children we must bear in mind the possibility that a chronic arthritis of one or more joints may be a

[1] PROGRESSIVE MEDICINE, December, 1900, p. 205. [2] Loc. cit.

manifestation of congenital lues, and the arthritis must be distinguished from tuberculosis. When there are no other evidences of the congenital taint the diagnosis is a very difficult one. It can be made in a similar way to that just discussed in the adult. The most important point to remember in the treatment of both forms of chronic luetic arthritis—acquired and congenital—is that the results are always better when the gumma formation is partially or completely excised; one must not depend upon medicinal treatment only.

The Joint Lesions of Syringomyelia. I find little to add to my extensive review of these interesting joint lesions.[1] Sokolow contributes a second article in conjunction with Nalbandoff,[2] in which appears the first Roentgen picture of this form of arthritis. The articular end of the humerus has been destroyed, and the end of the diaphysis was smooth (polished by friction). There was very little change in the ulna, except the sigmoid fossa was flattened. The head of the radius was partly gone. The interarticular space was very much increased. A collective review by Schlesinger[3] of the bone and joint lesions in syringomyelia has recently appeared.

Intermittent Joint Hydrops. Linberger,[4] in reporting two new cases of intermittent joint hydrops to the sixty-five previously recorded, adds nothing to the etiology or clinical picture of the disease previously given by Schlesinger, which I have discussed.[5] I am inclined to the view that one of Linberger's cases belongs to the form of symptomatic hydrops intermittens, because later in the disease this patient had attacks of gout in the other joints. The intermittent hydrops was present at pretty regular intervals after a slight trauma in the left knee for fifteen years. Every thirteen days this patient would have pain and swelling in the left knee, lasting two or three days; the knee then returned to normal. Now and then there would be an interval of a few months without an attack of hydrops. After fifteen years the attacks in this left knee were completely relieved by puncture and carbolic acid irrigation. The patient then suffered from a number of attacks of typical gout. Shortly after this attacks of intermittent hydrops of the right knee began. An apparently perfect cure followed a course of treatment at Carlsbad. The second case seems to be a typical idiopathic hydrops, in a male, aged twenty-three years. There was no etiological factor except exposure to cold and damp. The intermittent effusion was noticed in both knees about every ten or eleven

[1] PROGRESSIVE MEDICINE, December, 1900, p. 188.

[2] Mittheilungen aus den Grenzgebieten der Med. und Chirurgie, 1901, Band vii. p. 499.

[3] Centralblatt f. die Grenzgebiete der Med. und Chirurgie, 1901, Band iv. pp. 625 and 657.

[4] Beiträge zur klin. Chirurgie, 1901, Band xxx. p. 299.

[5] PROGRESSIVE MEDICINE, December, 1900, p. 195.

days. On palpation between the attacks slight hypertrophy of the villi could be made out, and some crepitation. The X-ray picture of both knees showed no disease of the bone. The patient was treated in von Bruns' clinic for two months with Bier's obstructive hyperæmia and other conservative methods, without result.

The Treatment of Non-tuberculous Joint Affections. In acute arthritis, whether secondary to trauma or not, we must at once exclude pyogenic infection of the joint or neighboring epiphyses of the bone. Every pyogenic infection demands immediate operative interference. This diagnosis should be based not upon the clinical picture, but upon the bacteriological study of the aspirated fluid. If pyogenic bacteria are absent operative interference is not indicated. In chronic arthritis we must exclude tuberculosis. In the early stages this can seldom be done on the clinical picture alone. The patient should be given tuberculin. The absence of a reaction is not positive, but it is very suggestive that the arthritis is of tuberculous origin. Nor if the patient reacts to tuberculin is it absolutely certain that the joint in question is a tuberculous one; but a reaction to tuberculin, with the rarest exceptions, indicates that there is a tuberculous focus somewhere in the body, and in the majority of instances arthritis is also part of the tuberculosis. In the absence of tuberculin reaction it is frequently justifiable to perform exploratory arthrotomy. This allows inspection of the joint, and we can remove a piece of the synovial membrane for histological examination and animal inoculation. The possibility of a non-tuberculous arthritis secondary to a small tuberculous focus in the epiphysis must be borne in mind. The so-called pretuberculous or irritative synovitis is described by Krause.[1] In the majority of such instances the patient would react to tuberculin. A Roentgen picture should always be made of the affected joint, but it must be emphasized that only gross lesions of the bone will be pictured. It is perfectly possible to have a small area of tuberculosis or purulent osteomyelitis, or even a new-growth, which, when entirely surrounded by thick, good bone, would not affect the Roentgen shadow. Having excluded pyogenic infection in acute arthritis, and tuberculosis in chronic arthritis, the treatment of the arthritis narrows itself to conservative and non-operative measures in the majority of instances. We must now think of the possibility of lues, which demands medicinal treatment, and in certain cases previously discussed, certain operative measures. In acute joint rheumatism and gout, rest is the most important local therapeutic measure during the acute attack. Large effusions should be aspirated. In these cases of acute arthritis which recover slowly from the acute attack,

[1] PROGRESSIVE MEDICINE, December, 1900, p. 203.

and in subacute and chronic non-tuberculous arthritis rest, and immobilization are the worst possible therapeutic measures. We must institute procedures to improve the circulation and aid in the absorption of the periarticular exudate before it becomes fibrous tissue. The therapeutic measures at hand are massage and passive motion, the application of heat of high degree (baking the joints), and Bier's obstructive hyperæmia. The last method of treatment has recently been discussed by Laspeyres.[1] I remember, when I was in Kiel, almost ten years ago, and visited von Esmarch's clinic with Bier, that almost every tuberculous and non-tuberculous joint was subjected to this form of treatment. Since then Bier has continued his method. Laspeyres, who was Bier's assistant for a number of years, gives us the experience of their clinic up to 1902. Although this experience has been most satisfactory, and Bier has frequently published his good results, there is very little in the literature to indicate that obstructive hyperæmia has found the place it deserves in the treatment of joint effusion. In gonorrhœal arthritis Bier never uses the obstructive hyperæmia until he has excluded the presence of the gonococcus in the joint affection. If the gonococcus is found arthrotomy and irrigation are first performed. Obstructive hyperæmia is used as a secondary measure. Observations demonstrated that it relieves the pain in many cases almost at once, and aids in the absorption of the periarticular exudate. In acute joint rheumatism and gout, obstructive hyperæmia is not indicated and of no special value in the acute stage. In gout we have no observations that this obstructive hyperæmia is of any therapeutic value in any stage of the arthritis. In rheumatism, however, if the arthritis in one or more joints does not recover with the cessation of the acute symptoms, obstructive hyperæmia should be tried, and in many instances will yield good results. In all forms of chronic non-tuberculous arthritis obstructive hyperæmia relieves pain, and after its use there is evidence in the greater mobility of the joint that absorption of the exudate in the soft tissues has taken place. We cannot expect from obstructive hyperæmia, heat massage, or passive motion any effect on the pathological processes in the cartilage and bone. The relief by these measures is due only to the beneficial changes produced in the soft tissues about the joints. As long as the pain, swelling, and fixation of the joint are due to inflammatory conditions of the soft parts of the joint only we can expect excellent results from Bier's hyperæmia and the other conservative methods mentioned. To the general practitioner Bier's hyperæmic method has advantages over baking the joint. The latter requires a rather expensive apparatus, and it is rather difficult to

[1] Centralblatt f. die Grenzgebiete der Med. und Chirurgie, 1902, Band v. p. 385.

employ it properly. The obstructive method is very simple in its application, the apparatus costs very little, and during the application the patient can walk; in fact, the results are better when the patient is allowed to be up and about. The application of the bandage has been described under Fractures. The limb should be bandaged above and below the affected joint. Above the affected joint the rubber bandage is then applied sufficiently tight to obstruct venous but not arterial circulation. This bandage can be left on from three to six hours. In some cases indicated by the immediate results we change the bandage two or three times a day. In other instances, one application a day is sufficient. With each change of the rubber bandage it should be applied at a new place around the extremity above the joint. The best results are obtained when, after the application of the rubber bandage, the skin over the joint becomes red and feels hot. Now and then vesicles will form in the epidermis. If the pain is increased the rubber bandage should be taken off. This method of treatment should be combined with massage, gentle passive motion, and the application of moist heat. The moist heat is best applied by wringing out the coarse bath-towels in very hot water. If there is contraction at the affected joint this method of treatment can be used in conjunction with extension. The entire limb should be firmly bandaged (a flannel bandage is the best) in the interval when obstructive hyperæmia is not being employed.

BENIGN AND MALIGNANT TUMORS OF THE BONE.

Much of importance has appeared recently on bone tumors which should be of great practical importance to the general practitioner, and many of the views held by the general profession need revision. First. There are tumors of the bone, distinctly benign, which can be recognized, if not by the clinical picture, always by the naked-eye appearance. These tumors do not tend to malignant infiltration or to metastasis. They can be cured by operations which preserve the limb and do not interfere with the continuity of the shaft of the bone. Second. Both periosteal and medullary sarcomata of bone vary in their malignancy. The character of the tumor can be recognized at the operation by its naked-eye appearances, and, according to the character of the tumor, operations of varying extent should be performed. In some sarcomata the disease can permanently be removed and cured by chiselling, preserving the continuity of the bone; in others a resection is sufficient; in other cases an amputation at a short distance above the disease. In the most malignant variety, exarticulation at the joint above the disease, with complete removal of all the muscles and their

attachments of that segment of the extremity, is absolutely essential. In this country, and perhaps among English surgeons, it seems to be the prevailing view that every sarcoma of the bone should be considered of equal malignancy, and the only operation justifiable in the attempt to cure should be an exarticulation at the highest joint.

The Ultimate Results after Operations for Sarcoma of the Long Pipe Bones. On this subject we have two recent and unusually complete articles: one by Kramer,[1] the other by Jenckel.[2] Kramer, in his monograph entitled "A Contribution to the Surgical Treatment of Malignant Sarcoma of the Hollow Bones," gives us not only the results in his own experience, but considers the reports from all large surgical clinics during the past ten years. Jenckel, on the other hand, confines his contributions entirely to the operative results for sarcoma of the femur, with a consideration of the entire literature on this subject. The conclusions of both these authorities, based upon their own experience and the most careful and critical study of the cases reported in the literature, come to views in direct opposition to those apparently held and published by many American surgeons.

John A. Wyeth,[3] of New York, in his paper read before the Philadelphia Academy of Surgery, April 1, 1901, takes the extreme view that in every case of sarcoma of the femur an exarticulation of the limb should be done at the hip-joint. He writes that every surgeon of large experience cannot fail to be impressed with the extremely malignant character of sarcoma as shown by the frequent recurrence either locally, in the stump, or internally. Wyeth collects 131 cases of amputations at the hip-joint in which his special method was followed, with an operative mortality of 10.6 per cent. (14 cases). Of 117 cases which survived the operation Wyeth was able to ascertain the ultimate result in only 82. In 51, at least (63 per cent.), the patients died from a recurrence of the disease, locally or internally. As many of the remaining cases have not been observed a sufficient length of time, Wyeth concludes that the percentage of the now apparently cured cases will be decreased. Of the 29 cases reported as cured, in 8 the duration of cure extends from four to nine years; the remaining cases, three years or less. As Wyeth does not give the number of patients in which the date of the operation was three years or more, one cannot compute the percentage represented by these nine cases which have remained well three years or more, or the twelve cases if we include those cured for three years. Wyeth records five of his own cases, only one of which still lives—a little more than three years after operation—and

[1] Archiv f. klin. Chirurgie, 1902, Band lxvi. p. 792.
[2] Deutsche Zeitschrift f. Chirurgie, 1902, Band lxiv. p. 66.
[3] Annals of Surgery, 1901, vol. xxxiv. p. 375.

he states that he sincerely believes that the cure in this case was due to his allowing the wound to become infected with pyogenic organisms. The majority of the surgeons who discussed Wyeth's[1] paper seemed agreed that in every case of sarcoma of the femur exarticulation of the hip should be performed, and that after the operation it was justifiable to inoculate the wound, if not with the streptococcus of erysipelas itself, at least with the toxins of the streptococcus and the bacillus prodigiosus, advocated by Coley in the treatment of malignant tumors. This inoculation is made with the hope of preventing a possible recurrence of the disease. In discussing Dr. Wyeth's paper I called attention[2] to the fact that there was much in the literature to indicate that sarcomata of bone were of different malignancy, and the extent of the operation could be varied according to the character of the tumor; that amputation was not always necessary, and that exarticulation at the highest joint was only indicated in the most malignant forms of sarcoma, or in other less malignant sarcomata on account of their position near the joint or their infiltration of the soft parts. This view is supported by a recent study of the operative results for sarcoma of the long bones treated in the Johns Hopkins Hospital clinic during the past thirteen years, and by the collective and most careful studies of Kramer and Jenckel.

Benign Giant-cell Sarcoma. Kramer[3] first calls attention to the difference in the malignancy of sarcoma of bone, and reports two cases of vascular giant-cell medullary sarcoma which have remained well eight and twelve years, respectively, after an operation which consisted of the removal of the disease from the medullary cavity by chisel and curette only, the continuity of the shaft of the bone being preserved. In the first case the giant-cell sarcoma was confined to the lower end of the right femur; the pain and swelling were of six months' duration. The tumor consisted of a red, vascular, fleshy mass circumscribed by uninfiltrated bone. The patient was a boy, aged sixteen years. The second patient was a girl, aged thirteen years. She had complained of restriction of motion at the shoulder and pain and swelling of the upper end of the right humerus for nine months. The tumor was circumscribed in the upper end of the humerus. These tumors, unfortunately, are comparatively rare; but a sufficient number are recorded in the literature by König[4] and others to establish, without a shadow of a doubt, their benign characteristics and their curability by conservative operations. The tumor is usually of slow growth, remains circumscribed, does not excite much new bone formation, and infiltrates very

[1] Annals of Surgery, 1901, vol. xxxiv. p. 584.
[2] Ibid., p. 594.
[3] Loc. cit.
[4] Progressive Medicine, December, 1899, p. 235.

slowly, so that it is surrounded by a wall of healthy bone. The new-growth is rather firm in consistency, quite vascular, and friable. In the tumor one seldom if ever finds any new bone formation. Now and then there may be a hemorrhage into the tumor, giving rise to the so-called *bone blood cysts*. In the wall of the cyst we can usually recognize with the naked eye an irregular zone of the fleshy giant-cell sarcoma; beyond this the bone zone. Under the microscope the tumor is made up chiefly of giant cells. It usually contains many blood-vessels. In the stroma between the bloodvessels and giant cells we see spindle and round cells in varying number. It is a tumor that is never gelatinous, nor does it become necrotic. If the tumor is disintegrated it is due to hemorrhage, and not to necrosis. The so-called epulis, a very benign tumor, so commonly observed arising from the outer layer of the periosteum of the jaw near its alveolar border, is usually a giant-cell sarcoma, and resembles in its gross and microscopic pathology the medullary giant-cell sarcoma of the long, hollow bones. Now and then we observe a circumscribed periosteal tumor of the long bones, composed chiefly of giant cells. This tumor, also, like the medullary giant-cell sarcoma and the epulis, is usually benign. Jenckel[1] mentions this tumor, and one of his cured cases of sarcoma of the femur belonged to this variety. The patient was a soldier, aged twenty-two years. In jumping he felt pain in the right groin and experienced a sensation as if something had torn. For two or three weeks he continued to suffer pain, not severe, in the right groin, then—four and a half months before he came to the surgical clinic—he felt a little swelling beneath the outer third of Poupart's ligament. This swelling had increased very little in size and gave discomfort only in violent motions. At the examination a tumor, about the size of a walnut, smooth in outline, could be palpated to the outer side of the vessels, below Poupart's ligament. It was fixed and apparently extended deeply toward the neck of the femur. An exploratory incision demonstrated a small cavity, filled with venous blood, containing loose minute spicules of bone. Some of the spicules were adherent to the cyst wall, which was about 2 mm. in thickness and of slightly vascular appearance. Under the microscope the wall proved to be a giant-cell sarcoma. Later, based chiefly on the naked-eye appearance, but reinforced by the microscopic examination, an operation of simple enucleation of the cyst wall was performed. It arose from the trochanter minor of the femur, and in the cancellous bone of this trochanter there was an extension of the cyst cavity, containing a little of the myeloid growth. This patient has remained well nearly thirteen years after the operation.

[1] Loc. cit.

Benign Bone Cysts. Besides the blood cysts due to a hemorrhage into a medullary giant-cell sarcoma Jenckel mentions the possibility of a blood cyst due to a hemorrhage into a cystic enchondroma. These cystic enchondromata, so well described by F. König,[1] we have previously discussed. Radical operations are not necessary beyond their complete excision. Beck[2] reports two cases of osseous cysts of the tibia, the origin of which is probably similar to that in König's cases. They are of additional interest because of the Roentgen pictures. The first patient was a boy, aged ten years, who gave a history of traumatism to the tibia eleven, ten, and three months before. After the second trauma he noticed a slight swelling at the upper end of the right tibia. After the last trauma the pain and swelling increased, and he walked with a limp. At the examination the upper half of the tibia was enlarged in spindle form. The surface of the tumor was smooth. On palpation most of the tumor was hard, but there were a few softer areas. Clinically, it resembles the picture of a medullary osteosarcoma, not uncommon at this age; and the upper third of the tibia is one of the most common sites for medullary sarcoma. This diagnosis was confirmed at the operation, and Beck found a cavity surrounded by a thin shell of normal bone. The cavity was lined by a rather thin membrane, projecting from which was a network of fibrous bands containing small particles of bone. The contents of the cyst consisted of dark, bloody, viscid serum. The lining membrane of the cavity was scraped and the thin, bony walls were collapsed. The skiagraph, two months after the operation, shows an almost complete bony repair. In the microscopic examination of the cyst wall and its contents no evidence of cartilage was found. The gross pathological picture, however, corresponds pretty closely to König's hemorrhagic cyst arising from the liquefaction of a misplaced island of cartilage. The second patient was a girl, aged thirteen years. Here we also have a history of trauma of eight months' duration, followed by swelling of the ankle. On inspection the lower third of the tibia was enlarged; the external malleolus was normal. A similar operation was performed, and the patient was well four and a half months later. Schlange[3] and Deetz[4] report cases of bone cysts in which, similar to König, they were able to demonstrate the cartilaginous origin. Beck is the first to publish Röntgen pictures. Corson,[5] of Savannah, reports a case of bone cyst of the lower end of the humerus. The patient was a girl, aged twenty-one years.

[1] PROGRESSIVE MEDICINE, December, 1899, p. 235.
[2] American Journal of the Medical Sciences, 1901, vol. cxxi. p. 666.
[3] Festschrift f. von Esmarch, 1893, p. 431.
[4] Beiträge zur klin. Chirurgie, 1900, Band xxvi. p. 120.
[5] Annals of Surgery, April, 1902, p. 505.

For two years she suffered with pain near the right elbow. One year previously the right humerus had been fractured at the junction of the middle and lower third, at the site of the previous area of pain. The trauma had been such a slight affair that it at once suggested the possibility of some medullary growth weakening the cortical bone at this part of the humerus. The fracture healed. The pain, however, continued, and for this reason the patient sought surgical advice. The lower third of the humerus was slightly enlarged and irregular. The Roentgen picture was not clear, and a provisional diagnosis of osteomyelitis was made. At the exploratory incision the typical thin shell of bone was found, the cyst was lined by the usual smooth membrane, and contained viscid, brownish fluid. Nothing was done except to pack the cavity with iodoform gauze. The cyst wall was not removed. The patient was perfectly well two years after the operation, although there is still a small discharging sinus. Without much doubt if the cyst wall had been removed at the operation the cavity would have filled with bone as in the other reported cases.

The Comparative Ultimate Results after Resection, Amputation, and Exarticulation for Malignant Sarcoma of Bone. Kramer[1] has ascertained the ultimate results in the thirteen cases of malignant sarcoma of bone treated by resection, including three of his own. He finds that five cases are cured three years and more; in three cases, in which at the operation infiltration of the muscles by the sarcoma was demonstrated, there was local recurrence in the stump, and although secondary operation was performed, the patients died of internal metastases. In five cases the patients died of internal metastases, usually to the lungs, without local recurrence. There have been two other cases of resection, but they have not been considered because the patients have been lost track of since the operation. This demonstrates 38 per cent. of cures and about 23 per cent. of local recurrence. Kramer has compared these results with those after amputation. He has taken the cases reported only from the large clinics and not isolated cases. Of course, these statistics are very difficult to summarize correctly, and the percentage of cures and local recurrences varies in the different surgical clinics, due most likely to the differing pathological variety, location, and infiltration of the tumors. Unfortunately, Kramer does not tabulate together the cases which have been observed three years or more, so that it is difficult, unless one took the time to go to the original and make a table for one's self, to make exact comparisons. Kramer, however, from his reading points out that the chief cause of death in sarcoma of bone is internal metastasis, undoubtedly present at

[1] Loc. cit.

the time of operation, and when present, of course, not influenced one way or the other by the method of operation. Internal metastasis usually causes death within the first year. In a few instances it has been observed from three to five years after operation. Wyeth[1] has also called attention to cases of late internal metastasis. Local recurrences seem to be a little more frequent, but only slightly so, after the resection operation; but this may be due to improper selection of the case for this method of operation. Internal metastases from local recurrences are much less frequent. In the majority of instances the local recurrence takes place in the soft parts, and usually within one year after operation, rarely after two years; in isolated cases it has been observed between three and five years after operation. The local recurrences are usually explained not by the incomplete removal of bone, but of soft parts. The few cases of local recurrence in the bone are explained by the possibility of metastatic foci of the tumor in the medullary cavity at some distance above the original growth. In view, however, of the many cures and the usual absence of local recurrence after the so-called low amputation, this possibility of medulla foci must be very rare. According to Kramer's observation, the results after resection and amputation are equally good if the tumor is confined to the bone, and, unfortunately, almost equally bad if there is muscle infiltration. Although *a priori* exarticulation with complete removal of the infiltrated muscles should give better results, yet statistics do not show this positively, probably because such tumors usually kill by internal metastasis. Mikulicz and Wiesinger[2] advocated resection, even if the soft parts were infiltrated, provided the vessels of the limb could be preserved and a functional extremity made after the resection. But further observations of these cases demonstrate, at least at this time, that resection of the bone should be confined to small, slowly growing, encapsulated central medullary sarcomata which have as yet not perforated the periosteum and infiltrated the soft parts, and which, without a doubt, extend up and down the bone so short a distance that the piece of bone removed will leave a limb of good function. This careful study of the entire literature demonstrates that resection is justifiable in certain selected cases, and that exarticulation is demanded only in certain very malignant infiltrating tumors, and that amputation is the rule in the majority of cases.

Jenckel[3] studies the same questions, but confines his observations to sarcoma of the femur. He takes exception to Kramer only as to the justification of resection; but as there have been but a few cases of sarcoma of the femur subjected to resection, and these cases have been

[1] Loc. cit.
[2] PROGRESSIVE MEDICINE, December, 1899, p. 238.
[3] Loc. cit.

those of the most extensive disease, Kramer's views, on account of his more extensive studies, should be given precedent over Jenckel's. Jenckel's figures, however, seem to be conclusive, that for tumors of the lower half of the femur exarticulation at the hip-joint gives no better results than high femoral amputation. Exarticulation is only necessary in sarcoma of the upper femoral shaft, or in cases with extensive muscle infiltration. In these cases of muscle infiltration not only should the bone be removed at the hip-joint, but every muscle of the femur should be completely excised, with its attachment to the pelvis. It is interesting to note that in 1890 Borck,[1] in his memorable paper before the German Congress, could not find a positive cure among 87 cases of exarticulation at the hip-joint for femoral sarcoma. However, some of the cases excluded by Borck at that time as of too recent date are living to-day. Jenckel studies the ultimate result in 35 cases which have been observed in the Göttingen clinic between 1880 and 1901. In 21 cases high femoral amputations were performed, in 10 cases exarticulations at the hip-joint. In 2 cases the tumors were inoperable, and only exploratory incisions were made. In 1 case a giant-cell sarcoma occurring in the form of a blood cyst was cured by resection of the tumor only, almost thirteen years.[2] The remaining case was a periosteal sarcoma treated by resection; the patient has been lost track of. Nineteen cases, or 61.5 per cent., died of internal metastasis; this corresponds very closely to Wyeth's 63 per cent. Thirteen cases died within a year, 4 within two years, and 2 within two years after the operation. Jenckel has observed no internal metastasis after three years. The operative mortality was about 6 per cent., 2 in 31 major operations. Four cases have remained well between six and fifteen years after operation; one of these cases, however, it must be remembered, was a benign giant-cell sarcoma. The cured cases were all sarcomata of the medullary variety of the lower third of the femur, and the operation an amputation of the upper femur and not an exarticulation at the hip. Jenckel finds recorded in the literature 7 cases of sarcoma of the femur which have remained free from a recurrence of the disease for periods varying from five to sixteen years. It is interesting to note that one of these cases died fifteen years after the first operation from a second primary sarcoma of the humerus. Another most remarkable recovery is an exarticulation at the hip for a metastatic carcinoma at the upper end of the femur secondary to excision of the breast for carcinoma. This case is reported by Rose.[3] I believe this is the only case of this character in the literature. I

[1] Archiv f. klin. Chirurgie, 1890, Band xl. p. 941.

[2] This case has been discussed on p. 153.

[3] Centralblatt f. Chirurgie, 1902, Band xxix. p. 17.

made a similar attempt for a metastatic carcinoma of the upper end of the humerus. The right arm was amputated above the shoulder, because of the intense pain due to the metastatic growth. A few weeks later the left breast and axilla were removed for the primary tumor. The patient lived about a year and a half in comfort, and died of internal metastasis, without local recurrence.

There are on record at least 22 cases of malignant sarcoma of the femur cured by amputation or exarticulation (Wyeth 12, Jenckel 10). These patients have remained well from three to sixteen years after operation. These figures do not include the reports of single cases. Unfortunately, we find, on studying the cases in detail, that in the majority of cases the tumor was situated in the lower half of the shaft. Sherman,[1] of San Francisco, records one of a few cured cases in which the tumor was situated in the neck of the femur. His patient was a boy, aged fourteen years, and remained well nine years after operation. In one of Wyeth's cured cases the sarcoma was situated in the great trochanter, and had infiltrated the soft parts. The patient had remained well three years after the operation.

The Ultimate Results after Operations in the Johns Hopkins Hospital for Sarcoma of the Long Bones. Since the hospital opened, in June, 1889, about 40 cases of sarcoma of the bone have been admitted to Dr. Halsted's clinic. We have for study of the ultimate results 29 cases in which the time since their admission to the clinic varies from three to ten years. The results of my observation of these 29 cases correspond with those of Kramer and Jenckel.[2] There is a distinct difference in the malignancy of sarcoma of the bone. The disease has been cured by resection and low amputation in properly selected cases. Local recurrence is very rare, death from internal metastasis is common. In studying the ultimate results we must first exclude the inoperable cases. In 6 patients, about 20 per cent., the disease was inoperable. The tumors were situated in the sacrum in 1 case, in the pelvis in 2 cases, in the scapula in 1 case, in the ribs with extensive infiltration of the chest wall in 1 case, and in the upper end of the femur in 1 case. Therefore, in only one instance in which a long bone was involved the disease was inoperable. In 23 cases the disease was apparently operable; but, unfortunately, six patients refused amputation. On the whole, these were the more favorable cases. The patients came to the clinic in the early stage of the disease. This experience is common in other clinics. If the tumor of the bone is small and gives little discomfort, it is difficult to persuade the patients to subject themselves to the mutilating operation of an amputation. It was this that first led

[1] Quoted by Wyeth.

[2] Loc. cit.

Mikulicz to attempt resection. This leaves us seventeen patients in which the tumors were apparently operable, and in which complete operations could be performed. Of these, eight patient are living and apparently well to-day. The duration of cures varies from three years and six months to nine years. One patient died a few months after operation from tuberculosis of the lungs. Unfortunately, there was no autopsy. These figures demonstrate at least 50 per cent. of cures. Four patients, about 25 per cent., died of internal metastasis—three within eight months after operation, one nineteen months after operation. In one patient only have we observed local recurrence in the stump. In this patient there was also pulmonary metastasis. In the remaining 3 cases the ultimate result is doubtful. One patient died of Bright's disease five months after operation; there was no local recurrence, but there may have been internal metastasis. Two patients have been lost track of since operation. I have studied the tissues in all of these cases, with the following results:

MEDULLARY GIANT-CELL SARCOMA. Four cases. In 3 the disease was situated in the lower end of the radius. These patients have remained well from three to seven years after operation, an amputation of the forearm. In 2 in which the disease was limited to the bone I believe an excision would have been possible and justifiable. In the fourth case the tumor was situated in the internal condyle of the femur. The leg was amputated at the thigh. The patient, a male, aged twenty-two years, had chronic gonorrhœa, with bladder and kidney complications. We are informed that he died five months later of nephritis.

PERIOSTEAL GIANT-CELL SARCOMA. Three cases. One is cured nine years after operation. The periosteal growth was situated at the lower end of the ulna, and was removed by resection. It was a typical vascular giant-cell sarcoma, with no new bone formation. It had infiltrated the muscle slightly, and had destroyed small portions of the shaft of the ulna. The patient has a very useful arm, and earns her living by ironing. In the second case the periosteal growth was situated on the head of the tibia. The circumscribed tumor had been present one year. It had recurred after partial excision eight months before. This patient is well August, 1902, one year after operation (an amputation at the knee-joint). Examined pathologically, the tumor, although it had infiltrated the skin, was circumscribed and did not infiltrate into the bone. I believe it could have been completely removed by resection without destroying the continuity of the tibia or interfering with the function of the knee-joint. In the third case the disease was situated in the middle third of the tibia. On account of the extensive infiltration of the bone the leg was amputated. The patient has been lost track of.

These observations on seven cases of giant-cell sarcoma demonstrate their benign character and the possibility of resection in selected cases.

MEDULLARY MYXOCHONDROSARCOMA. Four cases. Two patients have remained well six and seven years after operation: one an amputation at the shoulder for a tumor involving the upper end of the humerus and infiltrating the muscles; one an amputation of the upper third of the femur for a tumor of the lower end. The third patient died two and a half months after operation from tuberculosis of the lungs. In this case there was a huge tumor of the shaft of the femur, but at every point a bony capsule. Exarticulation at the hip-joint was performed. There may have been lung metastasis to explain the death. The fourth case was inoperable on account of its position in the body of the sacrum. This form of sarcoma is also apparently relatively benign.

PERIOSTEAL OSTEOSARCOMA (with much new bone formation). Three cases. One patient is living and well seven years after operation. The tumor was situated at the upper end of the humerus and had infiltrated all the surrounding muscles; the extremity was removed, with part of the clavicle and the head of the scapula and all the muscles of the upper extremity, leaving only skin flaps. The second case, confined to the upper third of the fibula, is of recent date. In the third case the disease, of long duration, on account of the infiltration of the chest wall was inoperable. The periosteal new-growths, characterized by a great deal of new bone formation, are also relatively benign. These benign characteristics I have also observed in tumors of the lower and upper jaw.

MEDULLARY SPINDLE AND ROUND-CELL SARCOMA. Six cases. One patient is well two years and six months after operation. The tumor was situated in the upper end of the humerus; although of considerable size, and disintegrated by hemorrhage, it was apparently pretty well encapsulated. It was removed by exarticulation of the upper extremity, with the scapula and clavicle and all the muscles. (This case is reported by Cushing in his article on "Shock," *Annals of Surgery*, September, 1902.) In a similar tumor of the scapula removed by shoulder-girdle exarticulation, the patient died six weeks later of internal metastasis. In a third case, an amputation at the thigh for a tumor involving the upper end of the tibia, there was local recurrence and internal metastasis in six months. Of the remaining three cases the result of one is doubtful, and two are of a recent date.

PERIOSTEAL SPINDLE AND ROUND-CELL SARCOMA (little or no bone formation). Three cases. Two died within a few months of internal metastasis. One situated on the pelvis was inoperable.

The relative malignancy of these spindle and round-cell sarcomata, whether they originate in the medulla or from the periosteum, is high.

They are characterized clinically by rapid growth, and on examination of the tumor one finds little if any new bone formation, but extensive bone destruction. Pathological fracture occurs early, also infiltration of the soft parts. I believe excision should never be attempted unless we fortunately observe the disease in its very earliest period.

MEDULLARY PERITHELIAL ANGIOSARCOMA. This apparently is the most malignant variety of sarcoma of bone. We have observed three cases. In one of the scapula the tumor was inoperable. The patient died of internal metastasis three months after the first signs of the disease. The second patient died in a few months of internal metastasis after an exarticulation at the shoulder-joint. In this case there had been pain for six months, and a swelling of but two and a half months' duration. The third case is of particular interest. This patient came to the hospital with a recurrent tumor in the stump, with the following history: There had been a traumatism about three years before; for two years he had suffered with much pain referred to lower third of the femur; one year ago, after but a slight trauma, the femur was broken at the junction of the lower and middle third. This clinical history should have been sufficient to indicate a medullary sarcoma. Treated for fracture, there was no union for seven weeks. Six months after the fracture the leg was amputated for non-union. The disease was apparently not recognized. The recurrent tumor involved the entire stump, and there was metastasis to the iliac glands. Although exarticulation and excision of the glands were performed, local recurrence was observed one month after operation. The patient is now under treatment with the toxins of streptococcus and the bacillus prodigiosus, and his physician writes that there is apparently some improvement.

I have studied the relation between the pathological variety and the ultimate result in tumors of the upper and lower jaw, and find practically the same relation as that just discussed in tumors of the long bones.

Clinical Diagnosis of Sarcoma of Bone. The ultimate results just discussed represent cases of bone tumor in which, as a rule, the patients came to the clinic rather late in the disease, and there was not much difficulty in the correct diagnosis. Operations, even at this stage, have fortunately yielded relatively good results. The percentage of cures is about one-third of all operable cases. The symptoms of the tumor, however, in the majority of cases have been present a considerable period of time, so that without much doubt the disease could have been recognized at a much earlier period; and it seems but fair to conclude that if these cases could be subjected to earlier operations, our ultimate results would be very much improved. It should be our

object to educate ourselves with the very earliest symptoms of malignant tumors of bone, so that our patients can have the benefit of an early operation.

There is a distinct relation between trauma and bone tumors. Persistent local pain, especially when situated near the epiphyses, should make one suspicious of trouble. I find that in the majority of my own observations, and those in the literature, localized pain is the common initial symptom. This pain may be present weeks, months, and in rare cases one or two years, before any tumor is noted. In medullary sarcoma, with hardly an exception, pain is the initial symptom.

This is easy to explain, because at first we have a new-growth in the medullary cavity surrounded by a firm, bony wall, producing great tension. Later the pain is relieved, because the new-growth infiltrates and absorbs the bone. In the majority of cases of medullary sarcoma the clinical history is as follows: Quite marked local pain referred to end of the bone. The appearance of a swelling after which the pain is less, or we have a history of pain, and then from a very slight trauma a fracture. Such a history should be considered almost pathognomonic of a medullary sarcoma.

In periosteal sarcoma quite naturally the tumor is observed very shortly after the pain. Now and then the swelling may be obscured by the muscle coverings. Pain and swelling of a bone should make one very suspicious of disease, the nature of which should be determined at once. There should be no procrastination, no conservative treatment until at least malignant disease is positively excluded. Pain and swelling are symptoms common to all diseases of the bone. In acute epiphysitis in children the clinical picture can usually only be confused with an acute arthritis. The local signs of inflammation associated with the general symptoms of infection are sufficient to exclude malignant disease, but this diagnosis can always be confirmed at the necessary operation. It is the differential diagnosis of the subacute and chronic affections that is more difficult. Most diseases of the bone, like tubercular epiphysitis, gumma, and sarcoma, originate in or near the epiphysis, and are quite frequently associated with secondary joint irritation. Thus the symptom-complex in their early stage suggests some form of chronic arthritis. For this reason, in every case of monoarthritis the possibility of a bone lesion should be borne in mind. In making the differential diagnosis in the early stages, the clinical history and picture should never be considered sufficient to exclude a bone lesion. Tuberculin, which has been discussed, should always be given. The most valuable information is obtained by the Roentgen picture. Carl Beck, in his article on "The Differential Diag-

nosis of Bone Lesions,"[1] reproduces some very interesting Roentgen pictures. Fig. 47 is a very good illustration of a medullary sarcoma

FIG. 47.

of the lower end of the radius. In Fig. 48 one could exclude any gross bone lesion. The irregularity of the articular cartilage at the

[1] Annals of Surgery, 1901, vol. xxxiv. p. 753.

lower end of the femur would suggest some chronic joint inflammation with secondary destruction of the cartilage, most likely tuberculosis. In the majority of instances a good Roentgen picture will give us the

FIG. 48.

key to the diagnosis. If one is in doubt, or if the Roentgen shadow of the bone is suspicious but not positive, an exploratory operation should be performed. Fortunately, the naked-eye appearances of the different

bone lesions are not very difficult to recognize, even in their early stages. If these principles in diagnosis dwelt upon by Beck and others are followed malignant sarcoma of bone should be recognized the moment the individual seeks medical advice. In the early stage of sarcoma, before it has given great discomfort or produced marked deformity, and often in the later stages, it is difficult to persuade the average patient to submit to an amputation. On the other hand, it is not difficult to persuade them to allow a resection of bone. For this reason the statistics on ultimate results are of great practical value, because they teach us that cures are possible by more conservative operations. And, without much doubt, these conservative operations will increase in number with the early recognition of sarcoma of bone and the better knowledge of the naked-eye appearance of the different varieties of both medullary and periosteal sarcomata.

Treatment of Malignant Tumors. In consideration of the recent views on the treatment of malignant disease in general, that the most extensive operation is justifiable and should be done in all cases, it is natural to think at first that a conservative operation for sarcoma of bone is a step backward. But it must be conceded that the operation problem differs not only with the locality of the primary tumor, but also with its pathological variety. In malignant tumors of the breast we have witnessed in the literature the change in the extent of the operation from the removal of the tumor up to the complete removal of the breast, both pectoral muscles, and the entire contents of the axilla and the supraclavicular fossa. But here the problem is different. The mortality and the mutilation of the most extensive operation is little if any more than the conservative operation, while the probabilities of a cure are tremendously increased by the extensive operation. It is undoubtedly true, and my recent studies on breast tumors confirm it, that tumors of the breast (carcinoma) differ in their malignancy, and if one has sufficient knowledge this difference can be recognized at the operation, so that it is possible to cure the less malignant and extensive carcinoma by less extensive operations. But the less extensive operation in this locality gives so little less deformity that there is no reason or justification to limit the extent of our operations for malignant tumors of the breast. The same is true in operations for epithelioma of the lip. Many cases can be cured by the excision of the lip only, but the mutilation of the more extensive operation—removal of the glands of the neck—is so little that every patient should be given the benefit of the doubt and these glands removed at the same time that the tumor of the lip is excised. But the operation problem in tumors of the bone is an entirely different one. The object of surgery is not only to cure, but, if possible, to cure without mutilation. Amputation should be the

last resort of surgery. While it is true that exarticulation at the highest joint would unquestionably most completely remove the disease, yet recent statistics of practically all the largest clinics of the world demonstrate that in one form of sarcoma the disease may be completely used without destroying the continuity of the bone, so that the function of the limb is not at all interfered with; in another by resection; in a third form by low amputation, leaving a stump better adapted for an artificial limb. It is only in the most malignant forms with soft-part infiltration that exarticulation at the highest joint is demanded. Yet, unfortunately even after this most extensive operation few cures are obtained, because in this variety of sarcoma associated with soft part infiltration internal metastasis has generally taken place, so that, as a matter of fact, the results of the more conservative operations are better than those of the most extensive, due, however, to no fault of the exarticulation, but to the nature of the original tumor.

SURGERY AND DISEASES OF THE MUSCLES.

On this important and interesting subject in special surgery one finds little even in the most modern text-books. Nevertheless, both primary and secondary affections of isolated muscles are quite frequently presenting themselves for diagnosis and treatment. The early clinical recognition of the disease is of the greatest importance. Two conditions present themselves for differential diagnosis: the various forms of myositis, primary or secondary, and the muscular and intermuscular benign and malignant tumors. One can see at once the value of a differential diagnosis, for in inflammations and benign tumors a much less extensive operative procedure is indicated. It would be a very unfortunate occurrence to amputate an extremity for a benign tumor or a tumor due to inflammation of the muscle. In many instances the diagnosis can be made from the clinical picture; if this is doubtful, the naked-eye appearances exposed by an exploratory incision will, with very rare exceptions, indicate the character of the disease. Primary sarcomata of the muscle are very rare tumors, intermuscular sarcomata originating from the connective tissue are not uncommon. Benign tumors are also rare. The various forms of myositis are not uncommon as compared with other diseases of muscle and the intermuscular tissue.

Polymyositis Ossificans Progressiva (multiple progressive ossifying myositis). This rare and hopeless disease is mentioned simply to be excluded from the differential diagnosis. The multiple hard tumors to be seen and felt in the various muscles of the body eventually lead in many cases to ossification of large groups of muscles, make the

diagnosis of little difficulty. One interested in the disease will find Rager's[1] article most complete. The entire literature, including the 54 cases so far reported, is fully and carefully considered. Figs. 49 and 50 well illustrate the multiple tumors and some of the contractions due to the ossifying myositis. We observe the contraction of the right forearm, which was due to the ossification of the biceps muscle.

FIG. 49.

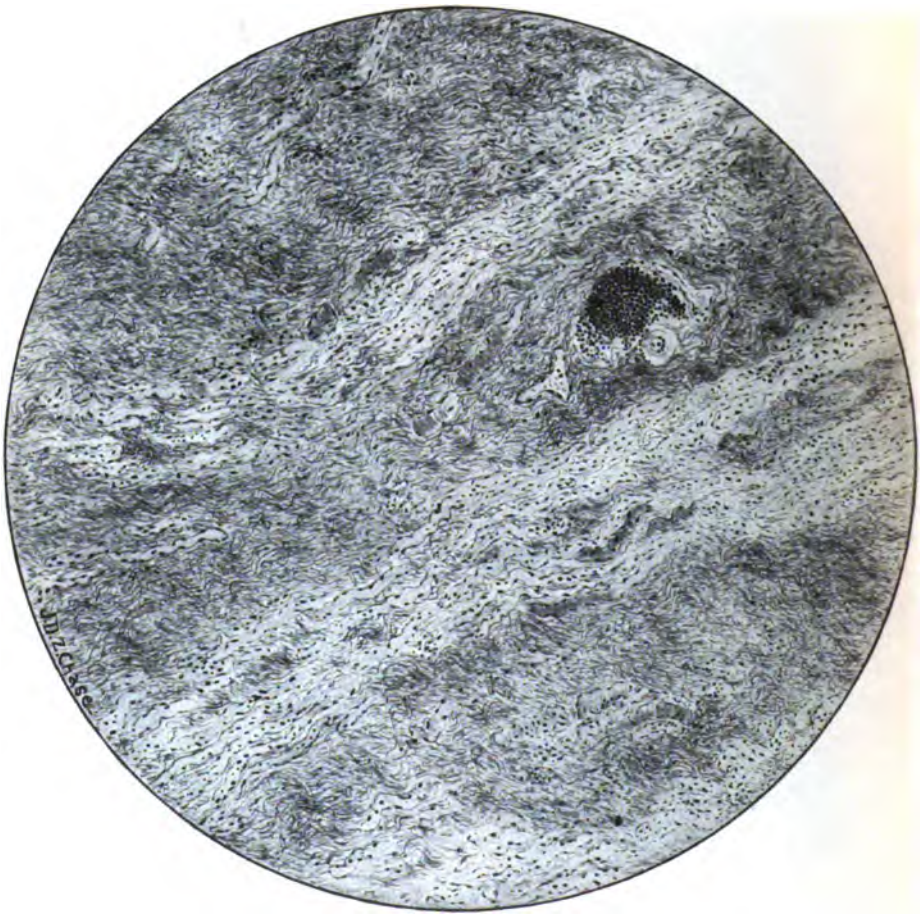
FIG. 50.

Myositis Fibrosa. Biggs[2] reports a very interesting case from the clinic of Dr. Frazier, of the University of Pennsylvania. The patient was a miner, aged twenty-four years. The previous history was negative as to any etiological factor except trauma. About four months previous to his admission to the hospital he received a blow on the right thigh by a piece of coal. At first there was little evidence of

[1] Zeitschrift f. Orthop. Chirurgie, 1901, Band ix. p. 380.
[2] University of Pennsylvania Medical Bulletin, December, 1901, vol. xiv. p. 353.

injury except local pain, which, at the end of the week, compelled him to stop working. The patient had been treated for rheumatism, and one physician considered it osteomyelitis. The clinical symptoms were local pain and swelling of the thigh. On examination the outer central portion was occupied by an irregular ovoid tumor. It was very hard, the skin over the tumor was indurated and slightly discolored and

FIG. 51.



Myositis fibrosa. Longitudinal section.

somewhat adherent. The mass was apparently fixed to the shaft of the femur. It was quite tender on palpation. The local pain was increased by muscular movements, and motions at the knee-joint were restricted. The X-ray shadow showed a normal femur. The shadow due to the tumor was slightly denser than that of the normal muscle, but not sufficiently dense to suggest bone. At the exploratory operation it was

found that the mass was in the quadriceps extensor muscle. It was evidently due to a change in the muscle itself. It was not encapsulated. The individual muscle bundle was firmer and paler than normal, and the intermuscular connective tissue was greatly increased and harder than normal. The mass was but slightly adherent to the periosteum, which was otherwise normal. This naked-eye appearance, so carefully

FIG. 52.

Myositis fibrosa. Cross-section.

described, excluded a new-growth, and for this reason, after the removal of some of the tissue for study, the wound was closed. After operation and the healing of the wound the patient was treated with massage, passive motion, and exercise. At the time of this report, a few weeks after operation, the pain was rapidly disappearing, the area of induration getting smaller, and there was very much less restriction of function of the muscle. Figs. 51 and 52 illustrate beautifully the

histological findings in this case. We see the great increase of fibrous connective tissue between the muscular bundles and the atrophy and beginning degeneration of some of the muscular bundles. The amount of round-cell infiltration is slight, and there is no histological evidence of bone formation. It is simply the picture of chronic interstitial myositis, with beginning degeneration of the muscles. Clinically, the picture is one of chronic inflammation rather than new-growth. The absence of fever and the rather chronic course (three months) would almost exclude a purulent inflammation. It differs from ossifying myositis in the slight involvement of the skin and the absence of the bony hardness of the tumor, and in the X-ray picture. In an ossifying myositis of four months' duration we would, in the majority of instances, have a distinctly bony shadow. As an etiological factor in this case the trauma is distinct.

I have recently observed a very similar case in which the naked-eye appearances and the histological picture are identical. The patient was a baker, aged forty-two years, and had been under treatment for diabetes for two years. His general condition was excellent, and there was but very slight polyuria, yet the urine contained a great deal of sugar. I could obtain no history of a direct trauma. The patient worked hard in the bakery, and was exposed to great heat. Five weeks before his admission he noticed a slightly painful and tender swelling on the flexor surface of the upper third of the forearm and slight restriction of the function of the flexor muscle. It had prevented him from working for about two weeks.

Examination. The swelling began 2 cm. below the bend of the elbow and extended to about the middle of the forearm. The skin was slightly red and œdematous, and apparently slightly fixed to the mass beneath. The mass was irregular and very hard, but not bony. The X-ray negatives showed no change in the bones, nor could I see that the mass produced any shadow. At the exploratory operation a similar picture to that described by Biggs was found, and microscopic sections of pieces of muscle removed were similar to the illustration by Biggs. In this case the clinical diagnosis of chronic myositis was made. The operation was performed, with the hope that a partial excision of the diseased muscle would relieve tension and improve the circulation, and for this reason not only check the disease, but aid in the rapidity of the resorption of the fibrous tissue. At the present writing, six weeks after the operation, the area of induration has almost disappeared, pain and tenderness are completely relieved, and the functions of the muscle are almost completely restored.

In both of these cases trichinosis, a very common cause of myositis, can be excluded. In Biggs' case trauma was undoubtedly the etiolog-

ical factor. In my case the cause is obscure. Unfortunately, in both of these cases there was no bacteriological study. I should recommend exploratory operation in similar cases. It can be performed under local cocaine anæsthesia, as was done in my case. This at once establishes the correct diagnosis. If the disease proves to be a new-growth it would allow an earlier complete excision; if the disease is the purulent form of myositis the pus would be evacuated earlier. In cases of myositis fibrosa I believe the incision associated with partial excision of the more fibrous parts of the muscle will be followed by more rapid resolution.

Primary Purulent Myositis. Honsell,[1] in reporting nine cases from the surgical clinic of von Bruns, in Tübingen, considers the entire literature up to date, and gives a very excellent and clear description of this disease. By primary purulent myositis we mean those cases of inflammation of single muscles leading to abscess formation which are not associated with any definite local infection or general infectious diseases; that is, the disease in the muscle can be compared to osteomyelitis. In both we must admit of some portal of entrance through which the bacteria reach the blood and later produce a local suppuration. The disease, as a rule, begins with slight general symptoms—fever, malaise, etc.—quickly associated with pain, tenderness, and swelling in some single muscle. If not operated on, the abscess in the muscle may rupture spontaneously. Now and then, as in osteomyelitis, the general symptoms are of such severity that the local signs are masked or not observed, and the patients die in a few days. At the autopsy the local area of suppuration is found. In the milder cases the differential diagnosis should not be difficult, but we must always bear in mind that the purulent myositis may be secondary to a suppurative lesion in a neighboring joint or bone or some near organ. The treatment consists in an early incision into the infected muscle and the exclusion of a neighboring focus, which if present should be treated in a similar manner. Now and then, if the operation is performed early in the disease, no definite abscess will be found. I have observed such a case. The patient, a male, aged twenty-one years, was under treatment for malaria in the medical wards of the Johns Hopkins Hospital. Without trauma and without apparent reason he began to complain of pain in the right thigh, quickly associated with swelling and tenderness. On the fifteenth day he was transferred to the surgical side.

Examination. There was fusiform swelling apparently in the rectus muscle, extending from the upper third of the thigh to the patella. The skin was normal. The mass felt hard and irregular. It was not

[1] Beiträge zur klin. Chirurgie, 1901, Band xxxi. p. 117.

boggy; it was quite tender. It had been associated with slight fever, although the malarial organisms had disappeared from the blood. At the operation a portion of the rectus and vastus externus muscles were excised. The naked-eye appearance differed somewhat from that described in the case of myositis fibrosa. The muscle was softer, more juicy, and vascular. There was a distinct fresh exudate, but no naked-eye areas of pus. The tissues were œdematous and the muscle bundles looked pale. The intermuscular connective tissue was thickened not by a new-growth of fibrous tissue, but by a rather fresh exudate. Under the microscope there was a distinct and marked collection of leucocytes between the muscular bundles, and the muscle fibre showed hyaline degeneration. The cultures and cover-slips were negative. I considered the case, from the clinical and histological findings, an early stage of primary purulent myositis. In all of Honsell's cases abscesses had formed, and he obtained pure cultures, in each case, of the staphylococcus pyogenes aureus. I have observed a second similar case in the biceps muscle of the left thigh. Clinically and histologically the cases were identical, except in the second case the myositis was apparently metastatic, from an infected wound of the right thumb. Unfortunately, there was no bacteriological study made.

Primary Myositis Ossificans. Recently there have been a number of interesting communications on this rather rare disease of the muscle. In the majority of instances trauma can be considered the direct cause. There is yet a difference of opinion as to whether the ossification between the muscles arises from the connective-tissue cells or whether it originates from pieces of the periosteum detached and misplaced at the time of the trauma. If the latter is true, the term primary myositis deformans is a misnomer. Nevertheless, the disease presents itself clinically as a muscular mass, and must be differentiated from other conditions in the same locality. This ossification is associated with two forms of trauma: first, slight but frequently repeated insults; second, a single but severe trauma.

Cases associated with frequent slight trauma are not very rare. For example, the so-called "rider's bone" in the adductor longus muscle, observed in cavalry soldiers; the "drilling bone," situated in the pectoralis major, observed in soldiers, due to the frequent contusion from the butt of the rifle; and quite a number of other ossifications in individual muscles associated with certain occupations or exercises in which the affected muscle is subjected to frequent insults. The more interesting cases are those following a single severe trauma.

Graf[1] reports a case from König's clinic in the Charité Hospital in

[1] Archiv f. klin. Chirurgie, 1902, Band lxvi. p. 1105.

Berlin. This patient, a man, aged fifty-seven years, received a severe trauma on the inner side of the right thigh. The patient was knocked down, but was able to get up and continue his work as a poleman on a raft. For the next three months he limped, and suffered with increasing pain on the inner side of the thigh associated with restricted motion at the hip-joint. Four and a half months after the injury he was confined to bed on account of the increase of the symptoms just mentioned.

Examination Eight Months after Injury. The right thigh was flexed 45 degrees, abducted 35 degrees, and rotated out. No motion was allowed at the hip-joint; there was no real shortening and no signs of disease about the hip-joint. Extending between the femur and the pelvis in the adductor muscles there was a hard, bony mass. The skin was normal. The patient was able to walk with two canes, but complained of great pain in the leg. Under ether, forced abduction separated the new bony growth from the shaft of the femur and allowed correction of the deformity. The patient was relieved, and refused further operative intervention. Graf does not commit himself as to the origin of the osteoid growth. It is important to note that the shadow in Graf's case of the new-growth of bone is of equal density with that of the shaft of the femur, and that the condition was of at least eight months' duration.

Vulpius'[1] case from the orthopedic clinic in Heidelberg is of special interest, first, because the area of ossification in the quadriceps muscle was distinctly separate from the periosteum of the femur. This was demonstrated without the shadow of a doubt at the operation. In addition, the centre of the tumor was occupied by a cyst, 12 x 4 x 2 cm. in diameter. The condition followed directly after a trauma, and the patient presented himself at the clinic seven weeks after the injury. The tumor, of bony hardness and irregular outline, was situated in the muscle. The skin was freely movable and normal; the tumor was movable from the femur. On palpation, one could elicit soft crepitation. Flexion at the knees was restricted. The operation consisted of complete excision. The contents of the cyst was a reddish-yellow fluid. The cyst was lined with a bluish membrane which projected into the cavity, dividing it into communicating chambers. The wall was composed of new bone of varying thickness, infiltrating the surrounding muscle. The infiltrated muscle showed an increase in the interstitial fibrous tissue and slight degeneration. Vulpius concludes from the study of this case that ossifying myositis may develop independently of the periosteum. His first case was of distinct periosteal origin. The patient presented himself, two months after the direct

[1] Archiv f. klin. Chirurgie, 1902, Band lxvii. p. 715.

trauma to the thigh, with a large bony mass in the quadriceps muscle adherent to the femur.

Schulz,[1] on the other hand, in reporting his cases from Garre's surgical clinic in Rostock, considers the condition to be of periosteal origin, because from his microscopic examination he demonstrated that the new bone formation was a typical periosteal ossification; yet in Schulz's case the bony tumor, containing a blood cyst similar to Vulpius' case, was not attached to the shaft of the femur. The bony tumor in the quadriceps femoris was of three weeks' duration, following a direct trauma. The mass was not adherent to the skin nor to the femur. The X-ray picture showed a normal shaft of the femur and a hollow mass of bone separate from the femur. At the operation in Schulz's case the new bone formation was slightly adherent to the periosteum of the femur.

Ossifying myositis containing in the centre of the new bone formation a blood cyst is rather rare. Rammstedt[2] was the first to report such a case. This case was clinically and pathologically similar to the two just described. In 1894 I operated on a blood cyst of the quadriceps femoris, the wall of which was composed of areas of ossification in the muscle.

The most careful histological study of post-traumatic ossification in muscle after a single trauma has recently been made by Berndt[3] from the surgical clinic in the city hospital in Stralsund, Germany. Berndt reports three cases, and is convinced that the ossification is from detached pieces of periosteum. His first case is of interest because the first X-ray photograph of the thigh, four weeks after the injury, exhibited no shadow, although a distinct bony tumor could be palpated. Three weeks later, during which time the tumor had become larger and harder, the shadow was observed, but of less density than the shaft of the femur. The bony growth was completely excised. This case is of additional interest, because the patient returned three years later with a similar area of ossification above the old scar, following directly after a second trauma; and it was also demonstrated by the X-ray photograph and at the operation that besides the new tumor there was a recurrence of the ossification to a slight degree in the old scar tissue.

The other microscopic illustrations of Berndt are not reproduced. They simply show that the majority of the new bone formation is of the periosteal type. Nevertheless, there is some bone formation from cartilage.

Clinically, these three forms of myositis (fibrosa, suppurative, and

[1] Beiträge zur klin. Chirurgie, 1902, Band xxxiii. p. 541.
[2] Archiv f. klin. Chirurgie, Band lxi. p. 153.
[3] Ibid., 1902, Band lxv. p. 235.

ossifying) should in the majority of instances be recognized. From this study of the literature and from my own cases I believe that an operation gives the best results, and at the same time allows from the naked-eye picture a positive differential diagnosis from a malignant tumor. According to Biggs, the area of myositis fibrosa should give a darker shadow than the normal muscle. This was not present in my case, which, however, was of but five weeks' duration, while in Biggs' patient the condition was of four months' duration. In ossifying myositis in the early stage there is no shadow in the X-ray. The shadow appears and grows denser up to that of normal bone, according to the duration of the trouble and the density of the bone formation. A hollow shadow would indicate a blood cyst, as seen in Berndt's first case. In a case reported by Rammstedt[1] the X-ray illustrates beautifully the rather faint shadow of an irregular bony growth in the brachialis anticus muscle slightly adherent to the shaft of the humerus. The trauma in this case occurred four months previous to the taking of the picture. Compared with an X-ray photograph of a periosteal osteosarcoma the differential diagnosis could easily be made.

[1] Beiträge zur klin. Chirurgie, 1900, Band xxviii. p. 1.

GENITO-URINARY DISEASES.

By WILLIAM T. BELFIELD, M.D.

INFECTIONS.

Gonococcus. The literature teems with additional cases proving that this bacterium may infect the blood current and produce metastases, with or without suppuration, remote from the site of the primary infection in the genital canal. Noteworthy among these are the observations of Reach[1] and Laurent,[2] who add to the five previously published cases three additional examples of gonococcus abscesses in the epididymis during acute gonorrhœa. These have always been found in the tail of the epididymis, in contradistinction to the infections by the tubercle bacillus, which always begin in the head of this organ.

Gonococcus infections of the ocular structures by metastasis through the blood current were discussed in the ophthalmic section of the British Medical Association.[3] Lamford described such infection of the conjunctiva, cornea, sclera, iris, choroid, and retina; he stated that metastatic gonorrhœal iritis is mild, has a tendency to recurrence, and is especially often found with arthritis. Yeld found 12 out of 159 cases of iritis to be metastatic gonococcus infections; of 32 men suffering from severe gonorrhœal infections of the joints, 5 had iritis of the same origin.

Ware[4] found gonococci in muscles adjacent to an infected knee two months after the urethral infection began.

Urbahn[5] asserts that some specimens of the gonococcus grow on agar, bouillon, and gelatin, contrary to the generally accepted belief.

Pseudogonorrhœa. To the many various purulent infections of the male urethra following suspicious connection, Waelsch[6] adds a type of which he has seen 5 examples. This pseudogonorrhœa is marked by long incubation (over two weeks), lack of severe symptoms, long duration, resistance to silver injections, and absence of the gonococcus.

[1] Centralblatt f. Krankh. der Harn u. Sexual Organs, 1901, p. 519.
[2] Journal des maladies cutan. et syph., 1902, No. 3.
[3] British Medical Journal, November 2, 1901.
[4] American Journal of the Medical Sciences, July, 1901.
[5] Archiv f. Augenheilk., 1901, No. 44.
[6] Prag. med. Wochenschrift, 1901, No. 43.

Malherbe[1] describes a case of staphylococcus albus infection of the male urethra, marked by relatively slight purulent discharge, severe pain, and healing in a few weeks. He suggests that it may be acquired from a mouth containing aphthæ or other such lesion by unnatural coitus. Johnston[2] reports another case with profuse purulent discharge.

Goldberg[3] reports a case of clinical gonorrhœa following coitus and caused by the streptococcus pyogenes.

Reichmann[4] reports a case of chronic urethritis without discoverable bacteria.

Nogues reported to the French Urological Association a case in which a subject of hypertrophic cirrhosis of the liver developed a urethrorrhagia without venereal infection; the discharge soon became bloody; later hemorrhages occurred from the nose and mouth and into the skin.

TREATMENT. The fact long recognized that some silver compounds have a distinct inhibitory effect on the growth of the gonococcus in the urethra has led to the synthesis of various compounds of this metal with albumin, which should secure penetration thereof into the affected tissues. Argonin, argentamin, albargin, nargol, and protargol are the best known of these, whose value as urethral injections has been more or less satisfactorily established; each has, however, left much to be desired.

The latest candidate for professional favor as a means of securing the antigonococcic effect of silver in the urethra is termed by its maker silver vitelline or argyrol. It is said to be a compound of silver with a proteid obtained from wheat, the metal constituting 30 per cent. of its weight. It is extremely soluble, dissolving in less than its own weight of water, is not precipitated by any of the tissue salts, and does not coagulate albumin—properties which favor its penetration into the tissues; it is moreover non-irritating, even in a 20 per cent. solution.

Christian[5] summarizes his experience with it in 38 cases of acute gonorrhœa, as follows: "The amount of urethral discharge is in the majority of cases at once lessened in a marked degree. The actual duration of the disease is shorter than is obtained by the use of any other silver salt. In our cases 38 were cured in from two to four weeks."

Swinburne,[6] after observation of some 350 cases of acute gonorrhœa treated with argyrol injections, reaches essentially the same conclusions.

[1] Annales des maladies des organes gen.-urin., 1901, No. 11.
[2] Arch. f. Dermatol. und Syphilis, Band lviii.
[3] Prag. med. Wochenschrift, 1902, No. 9.
[4] Journal of Cutaneous and Genito-Urinary Disease, September, 1902.
[5] Medical Record, September 27, 1902.
[6] Ibid., October 11, 1902.

After using this remedy for several months I consider it the most efficient silver preparation I have yet used in the local treatment of gonorrhœa; though my present experience is less decisive than that of Christian above quoted. It is evident that no injection can effect a radical and prompt cure of gonorrhœa, because no injection can possibly penetrate the many infected lacunæ and glands of this elaborately garnished canal; nor is it probable that any medicament will diffuse so far into the subepithelial tissues as the gonococci grow. Hence injections must necessarily be, as they always have been, but imperfect and unsatisfactory means of reaching the invading organisms. Yet this new silver compound seems less unsatisfactory than its predecessors.

In acute gonorrhœa it is well to have the patient make a daily visit to the physician, who administers an injection of a 20 per cent. solution of argyrol, which is retained in the urethra five to ten minutes; the patient is supplied with a weaker solution (2 to 5 per cent.), which he injects four times daily, retaining each injection as long as can be conveniently done. These solutions are not irritating; and the black stains produced on the underwear are removed by the usual laundering process. It is to be remembered that during the second week of the discharge the infection usually extends so as to involve the deep urethra, and that the injection must be made to follow the infection. To accomplish this result, a syringe holding at least one ounce is required (the "ear" syringes of hard rubber are admirably adapted to this purpose); and the patient must be taught to relax his cut-off muscle by strenuous efforts to urinate during this injection with the one-ounce syringe.

It will be noted that a slight purulent discharge persists after the gonococci have virtually disappeared; and that this discharge will be sooner arrested by the injection of some astringent—hydrastis, zinc chloride, or picric acid solutions—in alternation with the argyrol, than by the continuation of this latter alone.

Pyogenic Bacteria. Feltin[1] describes twenty-five bacterial varieties found in pus infections of the urinary tract; of these the most frequently occurring are the streptococcus, staphylococcus, bacillus coli, and B. pyocyaneus. The only bacterium at present known to be capable of invading the normal bladder is the proteus of Hauser; all other varieties infect the urinary tract only when the nutrition of its tissues, and consequent power of resistance, have been impaired through the irritation by foreign bodies, retention of urine from prostatic enlargement, tight stricture, kinking of the ureter by a displaced kidney, and other predisposing causes.

Feltin finds the bacillus coli more frequently in old than in new cases; he believes that it expels certain other varieties, especially the

[1] Centralblatt f. Krankh. der Harn u. Sex. Org., March, 1902.

pus cocci, which are more numerous in recent than in old infections. The B. pyocyaneus also drives the pus cocci out of the urinary tract.

Guisy[1] relates six cases, carefully observed, in which bacterial infection of the bladder occurred in individuals who had never been catheterized; all these patients developed cystitis while suffering from intestinal disorders—dysentery, hernia, constipation. The bacteria found were the colon bacillus, staphylococcus, streptococcus, micrococcus ureæ.

Halle and Motz[2] draw the conclusion, from a histological study of one hundred inflamed bladders, that the invasion of the connective tissue by pus bacteria is the serious feature of cystitis; the chronic interstitial cystitis is the refractory form.

Carlier[3] reports operating on a vesicorectal fistula large enough to admit the finger-tip, in a man aged thirty-four years. This had existed for twenty-seven years, and had originated in the spontaneous discharge of a vesical calculus into the rectum of the seven-year-old child. No infection of the upper urinary passages existed, though fecal matter was frequently discharged by the urethra, and colon bacilli were numerous in the bladder.

Tubercle Bacillus. The tendency toward conservatism in the surgical treatment of tuberculosis of the genital and urinary organs becomes annually more pronounced, while the operative results obtained by nephrectomy in cases of so-called primary tuberculosis of one kidney become steadily more favorable.

There is now general recognition of the favorable influence exerted upon tuberculosis of the seminal vesicles and prostate by the resection or excision of the primarily infected epididymis and vas deferens.

Garceau[4] collected 174 cases of operations upon the tuberculous kidney, making with Bangs' table (*Annals of Surgery*, 1898), and Facklam's collection (*Archiv für klinische Chirurgie*, 1893) a total of 415 cases. His analysis of this material results in the following conclusions:

1. Renal tuberculosis is rarely primary, but usually secondary to the infection in other organs, notably the mediastinal and mesenteric glands; hence an operative success does not warrant a favorable prognosis as to the course of the tuberculous infection.

2. The ureter should be removed with the tuberculous kidney.

3. Resection of the kidney is not justified by results.

4. While nephrotomy gives a smaller operative mortality than nephrectomy, yet the remote results of the infection prove nephrotomy the more dangerous treatment of the tuberculous kidney.

[1] Annales des mal. des org. genito-urin., 1900, p. 1067. [2] Ibid., 1901.
[3] Ibid., p. 1370.
[4] Annals of Surgery, October, 1902.

At the end of two years only 7 per cent. of the cases collected by Bangs, 8 per cent. of Facklam's, and 21 per cent. of Garceau's collection were in good health.

Horwitz[1] presents an analysis of 96 personal operations for the relief of tuberculosis of the testicle; his conclusions constitute an admirable summary of the present attitude of surgery toward this infection of the genital organs in the male, and are here reproduced.

1. A primary tubercular infection of either the epididymis or testicle may occur, the former being by far the more common.

2. A primary infection of the epididymis, secondarily that of the testicle, is more common than the descending one.

3. Primary involvement of either the epididymis or testicle usually takes place through the circulation, the soil being predisposed to the location of the tubercle bacillus either by a slight traumatism or by some infective condition which has given rise to inflammation of the organ, most commonly an attack of gonorrhœa.

4. Secondary tubercular involvement of the epididymis or testicle sometimes follows a primary focus of the disease in other portions of the body, more commonly in those organs that are in a direct anatomical connection with the sexual glands, such as the seminal vesicles, prostate, urethra, bladder, ureter or kidney.

5. The invasion of the testicle may be rapid, associated with acute inflammatory symptoms, an abscess soon developing; or the onset may be slow, the symptoms simulating those of either chronic syphilitic orchitis or malignant disease of the organ.

6. The tuberculin test should always be employed in doubtful cases where only one focus of the disease is known to exist.

7. In doubtful cases associated with hydrocele the fluid should be examined for the tubercle bacilli and inoculating experiments made.

8. The injections of either emulsions of iodoform or of sulphate of zinc into the diseased part are not to be recommended.

9. In all cases of encapsulated caseous nodules quiescent in the epididymis, epididymectomy should be performed.

10. Epididymectomy, together with resection of the vas deferens, is not attended by either atrophy of the testicle or sexual weakness.

11. The drainage of tubercular abscesses, followed by the use of the curette, is only to be employed where radical treatment is not permissible, as it is attended with more or less danger, and is generally satisfactory in its results.

12. In instances where the epididymis alone is involved, a resection of the diseased structure is all that is required; whether a partial or

[1] Journal of American Medical Association, June 21, 1902.

complete resection of the vas deferens is to be undertaken is still undetermined.

13. Double orchidectomy should be performed when both glands are diseased, provided there is not extensive co-existing tubercular infection of other organs.

14. Whether infected seminal vesicles should always be removed at the time that the epididymis or testicle is resected is a question open for discussion. From the fact that in a large majority of cases the removal of the primary seat of the disease is followed by a subsidence of the tubercular involvement of the vesicles, it is deemed wiser, as a rule, to wait and remove the vesicles later, if necessary.

15. Hygienic and climatic influences play as important parts after operations in fortifying the constitution against further invasion as they do in other tubercular conditions.

16. The antitubercular remedies are of great value in controlling the disease, and should always be employed in conjunction with whatever surgical procedure may be deemed necessary.

Bohdanowicz[1] reports two cases of tuberculosis of the epididymis, with softening, apparently cured by repeated aspirations of the pus and injections of a few drops of camphorated naphthol, as advised by Berck.

Thorndike analyzes 75 cases of tuberculosis of the epididymis and testicle collected from the surgical records of the Boston City Hospital. In 67 per cent. the patients' age was between twenty and forty years; in 18 per cent. the disease was bilateral; the epididymis alone was infected in 42 cases, epididymis and testicle in 32 cases; the disease reached the seminal vesicle in 16, and the prostate in 13 cases. One case presented the rare occurrence of tuberculosis limited absolutely to the prostate, the autopsy failing to reveal any pre-existent lesion.

THE KIDNEY.

Interest in the surgical treatment of renal disease centres especially about two morbid conditions—movable kidney and chronic non-infectious nephritis (Bright's disease).

Movable Kidney. Opposition to the operative relief of the troubles consequent upon unnatural mobility of the kidney is still considerable; the complete relief of many cases by special bandages and the escape of many kidneys from the anchorage made by surgical interference, constitute the argument. Watt[2] reports 18 cases of movable kidney, with

[1] Annales des mal. des org. genito-urin., June, 1902.

[2] Edinburgh Medical Journal, December, 1901.

distressing symptoms, relieved completely or practically by a bandage of lead supporting the entire abdomen. Rafin[1] proved by the ureteral catheter that the painful crises of floating kidneys are due, as Albarran contends, to retention of urine from kinking of the ureter; he found that when the kidney was dislocated (the catheter being in position) but little or no urine escaped; while reposition of the kidney to its normal position was promptly followed by free escape of urine.

Mobility of the kidney was the special subject for discussion by the French Urological Association,[2] in October, 1901, a discussion which elaborately reviewed previous knowledge of this subject, but made no material additions thereto. Tédenat reported finding 15 movable kidneys in 100 women, 5 in 100 men; in 120 cases mobility was found on the right side, in 4 on the left side.

It was generally agreed that 10 to 12 per cent. of all women are thus afflicted; that the large majority of movable kidneys are on the right side; that the condition is acquired; that it is most commonly found between the ages of twenty and forty years, and occurs independently of pregnancy, enteroptosis, and obesity. It is frequently the cause of intermittent hydronephrosis and pyelonephritis; the ureteral catheter is an important diagnostic aid. Operative fixation is the only satisfactory treatment, and is permanently successful in 80 to 90 per cent. of cases.

The well-known production of symptoms in organs remote, both anatomically and physiologically, from the kidney was thoroughly reviewed and emphasized; and the often difficult differential diagnosis between the tumor caused by a dislocated kidney with or without hydronephrosis, on the one hand, and a tumor caused by a distended gall-bladder, wandering spleen, colonic neoplasm, ovarian, uterine, or appendicial lesion on the other, was thoroughly discussed. The use of the ureteral catheter as a differential diagnostic measure was again advocated, especially by Albarran.

The most satisfactory method for the differential diagnosis of a dislocated kidney is that first published by Tuffier in 1899 (*Semaine Médicale*), namely, X-ray skiagrams of a metallic catheter introduced into the ureter to the kidney. The application of this method to the differential diagnosis of kidney lesions (including dislocations of the organ) has been made by Schmidt and Kolischer,[3] and Loewenhardt.[4] Illyes[5] publishes 5 cases with radiograms, in which this method was

[1] Lyon Médicale, September 29, 1901.
[2] Annales des mal. des org. genito-urin., November, 1901.
[3] Monatsschrift f. Urologie, July, 1901.
[4] Centralblatt f. Krankh. der Harn u. Sex. Org., August, 1901.
[5] Annales des mal. des org. genito-urin., March, 1902.

successfully used for differential diagnosis; one of these cases having been demonstrated in Budapest in 1900.

Among the new methods for fixation of the movable kidney, the mattress suture through the fibrous capsule only, described, used, and illustrated by Goelet,[1] is worthy of mention. By it the direct tension and consequent tearing out of the suture is avoided, as well as the damage to the kidney tissue inflicted by the usual sutures.

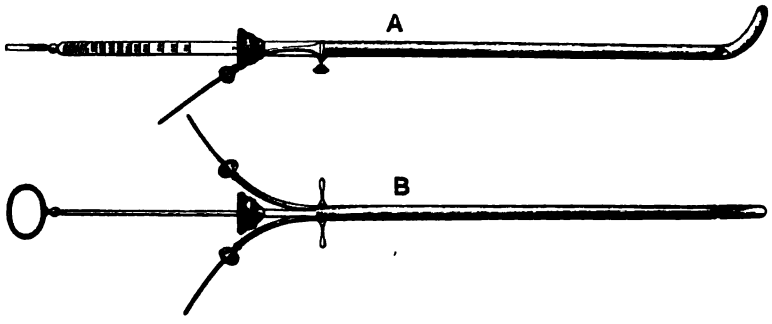
Edebohls[2] has performed nephropexy 261 times on 186 patients (of whom only 3 were males); 114 operations were unilateral, 68 bilateral at one sitting, 6 bilateral at two sittings. His test of success is that he cannot make the operated kidney recede out of reach beneath the ribs; by this test all his operations have been successful.

He anchors the kidney in front of the quadratus lumborum muscle, its upper pole projecting as far beneath the rib as its lower pole extends below the level of the iliac crest; he strips off a large piece of the fibrous capsule adjoining the quadratus lumborum, bares the corresponding surface of this muscle, and then leaves the two raw surfaces in apposition.

He thinks mobility of the right kidney is often intimately associated with disease of the gall-bladder; and thinks bilateral nephropexy is especially desirable when the dislocation of the kidney is complicated with chronic nephritis. He has operated on 13 such cases, with cure of the nephritis.

The Separation of the Urines furnished by the respective kidneys continues to occupy attention as a most desirable preliminary to any

FIG. 53.



Cathelin's vesical divisor, closed. A. Lateral view. B. Seen from above.

operation on the kidney. Catheterization of both ureters is admittedly the only accurate and reliable means to this end; but this measure requires special technical skill, and is even then sometimes impossible,

[1] American Medicine, September, 1902. [2] Annals of Surgery, February, 1902.

especially in the male. Hence, methods admittedly less accurate have achieved a certain vogue. The partition of the bladder into two compartments, into each of which a ureter opens, is a method first practised by Lambotte in 1891, and since modified by Neumann, Harris, and Downes; within the past year two new instruments intended to achieve the same result have been devised by Luys[1] and Cathelin,[2] respectively. The partition of the bladder in each of these is sought by the protrusion from the beak of a double catheter of a rubber sheet attached to a metallic rim. Each of these has been used, with more or less satisfactory results, by various Paris surgeons; but each would seem destined, like its predecessors, to a brief popularity and an early oblivion.

In PROGRESSIVE MEDICINE for December, 1899 (p. 133), the Neumann and Harris instruments were discussed, and certain anatomical considerations and clinical results were set forth, showing the fallacy of the conclusions based on the findings of either instrument. While some surgeons of experience still use and advocate the use of these devices, the general experience is that they frequently fail to separate the urines from the respective kidneys; and that, for the reasons presented three years ago and often confirmed since, the findings of either instrument should not be accepted as accurate until controlled and verified by cystoscopical inspection. Their use is justified only where ureteral catheterization is impossible or impracticable, and then only as a supplement to the cystoscope.

The Luys and Cathelin instruments, pictured and described in Guyon's journal, I have not yet examined; their employment is doubtless a less severe ordeal to the patient than is that of the Harris instrument, because the painful pressure of the rectal lever and catheter points is avoided. But their failure in a large percentage of cases to partition the bladder accurately can be as confidently predicted as was that of their predecessors, now amply demonstrated; and they, like the earlier instruments, complicate matters and confuse the operator by draining the bladder as well as the kidneys.

Catheterization of the ureters is admittedly the one reliable method for segregating the urines of the separate kidneys; and the earlier fear of infecting these canals has been proven unfounded by years of experience with ordinary aseptic precautions. In the female the introduction of the ureteral catheter is usually practicable; in the male, it must be admitted, the percentage of failures is still very large. Until improved instruments and technique give the operator better command of the ureteral orifices in the male the most available method for securing

[1] Annales des mal. des org. genito-urin., June, 1902. [2] Ibid., July, 1902.

information as to the functioning capacity of the respective kidneys seems to be that which combines the internal administration of methylene blue with the cystoscopic inspection of the ureteral orifices. Undue tardiness in the appearance of the blue at one of the ureteral orifices, and lengthened intervals between the peristaltic spurts from that orifice, warrant at least a suspicion that the kidney concerned is functionally impaired. The prolonged observation necessary to the satisfactory determination of this feature requires an irrigating cystoscope to keep the vesical contents transparent. In certain cases the ureteral orifice on one or both sides may be undiscoverable, even when it is spurting blue urine.

Chronic Nephritis. The surgical treatment of chronic nephritis is the latest advance of surgery upon the territory of internal medicine. In this connection a sharp distinction must be drawn between chronic nephritis of infectious origin and that of undetermined source—*i. e.*, "Bright's disease."

Through the cystoscope and ureteral catheter it has been definitely determined that chronic nephritis, the non-infectious as well as the infectious variety, may be unilateral, and therefore the legitimate object of surgical attack; and it has been amply demonstrated that a chronic infection of one kidney is frequently amenable to treatment by nephrotomy and drainage.

That the chronic lesions of a kidney due presumably to toxic or irritant elements in the blood, should be likewise curable by nephrectomy, splitting, or removal of the renal capsule, seems *a priori* less plausible. Yet this is the assertion made by several surgeons of experience during the past year.

Rovsing[1] reports the surgical treatment of 17 patients suffering from chronic nephritis. Of these 9 were of non-infectious origin, their urine being sterile; in 7 of these there was found a fibrous perinephritis, by which compression of the kidney, with resulting pain and hemorrhages, was induced. The surgical treatment consisted of liberation of the kidney from its compressing sheath of fibrous tissue, with or without nephrotomy; and the results were 8 complete cures and 1 death. The fatal case was one in which nephrotomy also was performed; he considers this incision of the kidney usually unnecessary and always dangerous if the opposite kidney also is diseased. Of the 8 infectious cases 5 were subjected to nephrotomy and 3 to nephrectomy (because of severe hemorrhages), with uniformly good result.

Pousson[2] reports operating in the same way on 6 cases of chronic

[1] Semaine Médicale, June 18, 1902.

[2] Annales des mal. des org. genito-urin., May, 1902.

Bright's disease; the results were great amelioration of symptoms in 4 cases, death in 2. He also operated on 4 cases of acute infectious nephritis, with 2 recoveries and 2 deaths; and collects reports of 19 other operations with 16 recoveries and 3 deaths.

Pousson also calls attention to the reflex inhibition of the function of one kidney by disease of the other, especially when this latter is a septic infection; and he finds in this a forcible argument for early interference.

Escat considers that the chief danger from a unilateral pyelonephritis is not the infection itself, but this inhibitory influence on the opposite kidney, which may result in uræmia without actual lesion of the second organ. He narrates 2 cases of pyonephrosis with uræmia; in one the diseased kidney was removed, with prompt cessation of the uræmic symptoms; in the second instance operation was refused and death from uræmia followed.

The reflex inhibition of the function of one kidney by disease of the other is well shown in cases of calculus anuria; and the arrest of the renal function by certain septic toxins is also well known. Hence the dangerous influence upon the opposite healthy kidney by unilateral pyelonephritis is most plausible.

Edebohls[1] adds to his earlier report[2] his experience with 18 cases. He was led to undertake the operative cure of chronic Bright's disease by the observation that in several cases the performance of nephropexy was followed by complete disappearance from the urine of albumin and casts that had long previously appeared therein. The first case of this category was operated on November 29, 1892, the fifth April 1, 1897. The first operation undertaken for the deliberate purpose of healing chronic Bright's disease was performed January 10, 1898; this patient was radically cured, and so remained at date of this report, nearly four years later.

The present article contains the tabular histories of 18 cases operated on for the purpose of relieving chronic Bright's disease. The patients were all women, between nineteen and forty-five years of age, averaging about thirty years. Thirteen were afflicted with chronic interstitial nephritis (9 unilateral, 4 bilateral), 2 had chronic parenchymatous nephritis, and 3 chronic diffuse nephritis (bilateral in all 5 cases).

In 14 cases both kidneys were operated on, in 12 at one sitting, in 2 at two sittings; in 4 cases only the right kidney was diseased and operated on. In 9 cases the disease was discovered shortly before operation; in 9 cases its existence had long been known (six years or

[1] New York Medical Record, December 21, 1901.
[2] PROGRESSIVE MEDICINE, December, 1900, p. 77.

less), and the usual symptoms of such disease, including uræmia and dropsy, had been observed.

Of 12 cases operated on a year or more before the report, 8 were radically cured, 3 had disappeared from observation, 1 was merely improved; of 4 cases operated on within six months, 2 were cured and 2 improving; the remaining 2 cases of the 18 were operated on too recently to justify conclusions.

The operation performed by Edebohls consists of the removal of the fibrous capsule of the kidney from the entire organ. He considers the favorable effect probably due not to relief of tension in the kidney, but to the improved blood supply to the cortex of that organ secured by anastomoses with surrounding tissues; that the operation is analogous to Morrison's for the relief of cirrhosis of the liver by securing anastomoses with the diaphragm.

Delbet[1] contributes an experimental study on contusions and lacerations of the kidney, and also a most comprehensive résumé of the cases recorded, some 320 in number.

THE URETER.

Calculus. Leonard[2] calls attention to the frequency of calculus in the ureter as revealed by the Roentgen ray, and the rarity of its discovery by other diagnostic means. Of 254 cases examined by this method because suspected of urinary lithiasis, one or more calculi were found in 73 individuals; and the clinically important fact is related that in 47 of these 73 the stone was formed in the ureter, while in only 26 was it discovered in the kidney. In other words, calculus in the ureter is more frequent than renal stone in the proportion of 3 to 2. Leonard emphasizes the frequency with which ureteral calculi are found by the X-ray in the absence of the usually accepted symptoms of their presence and the danger to the kidney of these undetected stones in the ureter. He also narrates cases in which the symptoms pointed to other well-recognized conditions, including appendicitis. He insists again that a negative result furnished by a skilful X-ray operator may be safely accepted as absolutely excluding renal and ureteral calculus.

This last statement has not yet received general indorsement; for instance, Cabot,[3] in discussing Leonard's paper, states that he has known instances in which kidney stones were removed that the X-ray had failed to detect. He remarks, moreover, that the lower portion of the ureter lies within the pelvis, whose osseous structure prevents

[1] Annales des mal. des org. genito-urin., 1901, p. 805.
[2] Journal of American Medical Association, October 18, 1902.
[3] Ibid., October 25, 1902.

Dislocated mobile kidney; metal probe in ureter, curved downward at upper extremity into renal pelvis. (Radiogram by W. C. Fuchs, Chicago.)

To face p. 189.

the detection of calculi within it, except under especially favoring circumstances. Young[1] mentioned a case in which a large renal calculus escaped detection by the X-ray because it was above the level of the plate employed. All agree, however, that the Roentgen ray is indispensable in the differential diagnosis of ureteral lesions.

Valve Formation. Morgan[2] describes a carefully observed and operated case of valvular formation in the ureter below the level of the upper end of the seminal vesicle in a patient aged twenty-one years; there was dilatation of the ureter above this valve.

Catheterization of the Ureter. To the obvious advantages of introducing a catheter into the ureter—such as securing the urine from the corresponding kidney uncontaminated by other fluids, detecting strictures and possibly calculi, draining hydronephroses both as a curative and as a diagnostic measure, irrigation of pyonephroses, etc.—some new functions have been added. The X-ray delineation of a metallic probe introduced into the ureter has been shown by Schmidt and Kolischer, Loewenhardt, and Illyes to be a valuable diagnostic aid in the differentiation of renal tumors and dislocated kidneys from other conditions. That a skilful surgeon may fail to make this distinction without such aid, is illustrated in 2 cases reported by Holmes.[3] In each there was a tumor in the region of the gall-bladder, icterus, and normal urine; but laparotomy revealed a normal gall-bladder and a diseased kidney —cystic in one case, movable in the other.

Albarran[4] advises the use of a ureteral catheter *à demeure* to prevent or cure fistulæ after nephrotomy; he has allowed the catheter to remain in position from eighteen to twenty-four days without harm. Eight fistulæ thus treated closed in one to four days, six of them permanently.

Kelly[5] advises that the ureteral catheter may be introduced and left in position as a preliminary to nephrotomy; when the kidney is exposed its pelvis and calyces can be distended with water advantageously.

Stockmann[6] reports 5 additional cases of pyelitis cured by irrigation through the ureteral catheter.

THE BLADDER.

Cystitis. That bacterial infection of the bladder—cystitis—is usually secondary to a pre-existent impairment of the vesical tissues, is now generally recognized; that the diagnosis must consist in discov-

[1] Journal of American Medical Association, October 25, 1902, p. 1031.
[2] Annals of Surgery, October, 1902.
[3] Journal of American Medical Association, July 20, 1901.
[4] Presse Médicale, 1901, No. 84.
[5] British Medical Journal, February 1, 1902.
[6] Wiener klin. Rundschau, 1901, Nos. 44 and 45.

ering this prior lesion, and the treatment of cystitis in removing such lesion, are obvious corollaries. Progress in the treatment of cystitis is therefore based on additional knowledge as to the causes which make it possible. To the long list of familiar causes—stricture, enlarged prostate, stone, tumor, tabes dorsalis, myelitis, etc.—Albarran and Guillain have added syringomyelia. They examined 2 cases of this disease with the cystoscope for Marie; in 1 they found a trabeculated bladder, chronic cystitis, and an ulcer measuring 1½ by 1 centimetre behind the trigonum; both patients suffered from hæmaturia and strangury. In 3 other subjects of this disease, who made no complaint of bladder symptoms, chronic cystitis was found. They ascribe these lesions to trophic disturbances. Blocq, in 1887, described a case in which ulceration of the bladder with perforation and fatal peritonitis occurred. Margoules[1] describes 3 cases of cystitis, apparently due to syphilis, because, after the failure of various modes of treatment, all were promptly cured by internal medication for that disease. In 2 cases there was hæmaturia; in 1 the cystoscope revealed an ulcer, in another a neoplasm composed of three small tumors.

Ulcer. Schmidt[2] reviews the subject of vesical ulcer, with a report of 5 cases treated by himself. Exact diagnosis must necessarily be made by means of the cystoscope, since no symptom is pathognomonic. Schmidt has secured the healing of ulcers by electrocauterization through the operating cystoscope.

Hypertrophy. Hist[3] discusses the cause of vesical hypertrophy in cases of tabes and of injury involving the posterior columns of the cord. He states that the vesical hypertrophy common in such cases is not due to hypertrophy of the sphincter (which does not exist), but to an impairment of sensation whereby co-ordination between sphincter and detrusor is impaired, and the work of the detrusor correspondingly increased. He states that trabeculation of the bladder may be one of the early results of tabes.

Exstrophy. Peters[4] reports 3 additional cases operated by his extraperitoneal method, with 2 recoveries and 1 death; the latter occurred on the fifth day after operation, and was due to ascending infection of the kidneys. His operation is stated to combine the peculiar advantage of Maydl's—the avoidance of injury to the ureter and its vesical orifice—with the added safety of extraperitoneal operating. The fatal case showed complete absence of peritoneal injury or infection; the recovered patients retain urine comfortably and completely for several hours.

[1] Annales des mal. des org. genito-urin., April, 1902.
[2] Journal of American Medical Association, July 19, 1902.
[3] Centralblatt f. Krankh. des Harn u. Sex. Org., March, 1902.
[4] Canadian Journal of Medicine and Surgery, April, 1902.

Extirpation. Harris[1] reports an extirpation of the prostate and the greater part of the bladder for malignant disease, with operative recovery and subsequent death from croupous pneumonia. He lays stress upon the retention of even a small part of the bladder wall and implantation of the ureters into this fragment; the bladder epithelium is rapidly extended from this fragment, and there is thus produced a small substitute bladder which offers much better protection against ascending infection of the kidneys than is furnished by any method of ureteral implantation into the bowel.

Rupture. Havas[2] reports another case of spontaneous rupture of the bladder in a man, aged fifty-five years, who had had chronic retention of urine from prostatic enlargement.

Fonstanos[3] observed a case of complete retention of urine from prostatic enlargement for twelve days; the bladder was distended to a level five fingers' breadth above the umbilicus, without rupture.

Jouon[4] presents a synopsis of the clinical history of 100 cases of extraperitoneal laceration of the bladder consecutive to fracture of the pelvic bones.

Incontinence. Albarran and Cathelin reported to the French Urological Association 15 cases of urinary incontinence treated by epidural injections of serum (15 c.c. to 20 c.c. each), or of cocaine (1 c.c. each of a 2 per cent. solution). Usually two or three injections were made, separated by a day's interval. In most cases prompt improvement followed the first injection. Among these cases were five infants, of whom three were cured immediately, and two improved; and 3 cases of complete incontinence from urinary tuberculosis, with one cure. Reynes[5] cured a case by a single epidural injection of 1 centigramme of cocaine.

Calculus. Frisch[6] draws conclusions from personal experience in 400 operations for vesical calculus; in 306 cases the stone was crushed, in 94 removed through a suprapubic incision. He thinks that the crushing operation should be done always if practicable; of his 306 cases, 2.6 per cent. died, and 8.2 per cent. showed recurrence; while of the 94 sections, 12.7 per cent. died, and 12.8 per cent. showed recurrence.

Serginewsky[7] presents a lengthy review and discussion of the geographical distribution of urinary lithiasis. He concludes that it

[1] Annals of Surgery, October, 1902.
[2] Pest. Med.-Chir. Presse, 1901, p. 1030.
[3] Annales des mal. des org. genito-urin., March, 1902.
[4] Ibid., September, 1902. [5] Ibid.
[6] Wiener klin. Wochenschrift, 1902, Nos. 13-15.
[7] Annales des mal. des org. genito-urin., March-June, 1902.

is certainly endemic in certain limited areas; but that no reason for this—either in water, food, or environment—has yet been revealed, except that in Egypt the frequency of vesical calculus is evidently in part due to the entrance of the Bilharzia parasite into the urinary tract.

Patent Urachus. Imbert[1] describes a congenital umbilico-vesical fistula in a girl, aged six years, which he excised completely through an abdominal incision, with recovery.

THE PROSTATE.

Hypertrophy. The etiology of prostatic hypertrophy is discussed by Greene and Brooks[2] on the basis of a histological study of 58 senile prostates. They corroborate the conclusions drawn by Ciechanowski from his elaborate investigations (reviewed in PROGRESSIVE MEDICINE, December, 1901, p. 110). They consider the prostatic hypertrophy so common in the aged as the result of chronic prostatitis, which in turn most frequently arises from chronic posterior urethritis, of whatever cause. True neoplasms of the prostate are rare, and are not concerned in the production of prostatic hypertrophy; while carcinoma is apt to develop in the hypertrophied prostate as a result of the chronic inflammatory process.

As inflammation is essentially a reparative and remedial process, aroused by extraordinary stimulation of the tissues concerned, the etiology of a chronic inflammation is in nowise revealed by a study of its anatomical details. There are good reasons for suspecting that the cause of prostatic hypertrophy will some day be found in a perverted testicular secretion.

Treatment. The medical treatment of this lesion has made no especial progress; urotropin internally, and silver nitrate or argyrol locally, remain the most efficient means for arresting the secondary pus infection of the impaired bladder tissues—that is, the cystitis.

The operative treatment has been zealously prosecuted by many surgeons, with results that may be thus summarized:

TREATMENT BY CAUTERY from the rectum is advocated by Negretto.[3] He uses a speculum, tenaculum, and Paquelin or galvanocautery. The rectum is emptied by a previous purge and by glycerin enema; general anæsthesia is preferred, but not essential, since an alcoholic solution of chloral with morphine renders the operation almost painless. The patient is placed in the perineal lithotomy position with pelvis elevated, and the rectum packed with gauze above the prostate; the speculum is

[1] Société de Chirurgie, November 20, 1901.
[2] Journal of American Medical Association, April 26, 1902.
[3] Gazz. Osped., August 10, 1902.

withdrawn, the tenaculum is inserted into the centre of the gland, which is drawn slightly downward. The speculum is again introduced, and the cautery applied around the tenaculum, superficially unless hypertrophy is great, in which case the point is inserted into the substance of the gland. A Nélaton catheter is left in the urethra for ten or twelve days; on the sixth or seventh day a purgative dose of oil is given. It is asserted that no ill-effects have been observed, but great shrinkage and relief of symptoms have invariably followed.

THE SO-CALLED "SEXUAL" OPERATIONS—castration and vasectomy —have lapsed into innocuous desuetude.

THE BOTTINI RESURRECTION has been followed by a virtual reinterment of this unsurgical procedure, though it still finds a few advocates. It is now generally recognized that the cases in which the Bottini operation scores its greatest successes can be benefited without the dangers incident to this operation; while as a standard measure for the relief of prostatic hypertrophy in general it has no pretensions whatever. The various efforts made to so modify the Bottini instrument as to make this operation a rational procedure have failed; and the latest improvement, proposed and pictured by Schlagintweit[1]—a heated wire emerging from the concave surface of a sound, to the curved extremity of which it bears the same relation as the bowstring does to a bow —seems a dubious improvement.

PROSTATECTOMY. 1. The suprapubic excision of tissue masses constituting the enlargement of the prostate was first intentionally performed through a suprapubic cystotomy by the present writer in 1886; and 2 such cases were recorded by him before McGill—to whom the credit is usually given, even by American writers—performed his first operation. Suprapubic prostatectomy combined with perineal urethrotomy, while entirely satisfactory from the anatomical standpoint, gave a large mortality from septic infection, and for that reason failed to secure general adoption. In 1889 Dittel proposed, and Kocher soon afterward twice executed, the exposure of the rectal surface of the prostate by a perineal incision and separation of the two organs; after which the posterior prostatic capsule was incised and the prostatic masses excised, without opening the urethra or bladder (though Kocher unintentionally opened the urethra in one case).

This method was unsatisfactory because it failed to detect and remove the intravesical portions of the hypertrophied gland and to drain the septic bladder.

Various combinations of the suprapubic and perineal avenues of approach to the enlarged prostate were devised by different surgeons:

[1] Centralblatt f. Krankh. des Harn u. Sex. Org., June, 1902.

Nicoll (1895) combined perineal enucleation (after Dittel) with counter-pressure from above through the opened bladder, but did not open the urethra; Alexander (1896) added to this a perineal urethrotomy; Bryson (1898) made a perineal enucleation with a suprapubic incision into the prevesical space for counter-pressure, but without opening the bladder above; Syms (1899) proposed perineal enucleation, securing counter-pressure by opening the peritoneum above the bladder, but not incising this viscus.

Each of these operations found advocates, and each furnished unquestionably good results, though still leaving something to be desired.

PERINEAL PROSTATECTOMY with enucleation of intravesical masses through the incised prostatic urethra, was—like the suprapubic prostatectomy—first performed by the present writer[1] in 1894. The perineal incision followed that of Dittel; but the prostatic urethra and vesical neck were incised and the enucleation of lateral masses made through the incision; thorough drainage of the bladder was secured.

Murphy[2] reports 8 cases of perineal prostatectomy with operative and functional recovery, and describes the last operation as follows: Lithotomy position of the patient; inverted Y-incision in perineum from junction of posterior fold of scrotum back to the rami at a level with the anus; rectum pushed away from prostate with finger, and deep retractors used to expose field of operation; capsule of gland incised parallel with urethra and separated from gland by finger and blunt dissection; right lobe grasped with small hook retractor and drawn down and out and then grasped with second hook retractor, rolled out from behind forward and separated from the bladder with the finger, and isthmus divided. Left lobe is treated in like manner. Middle lobe is shelled out and removed with posterior wall of prostatic urethra; isthmus not disturbed. Rubber drainage-tube was passed through perineum into bladder, and soft catheter through urethra.

Murphy's conclusions are as follows:

1. From the clinical reports and experience, it seems evident that in extreme cases prostatotomy is the operation of election.

2. It appears evident that in the hands of safe, far-seeing, informed practitioners few cases will now be allowed to progress to this extreme condition before radical means are resorted to for permanent relief. The practice of to-day should be timely practice.

3. Continued use of the catheter is a menace to life, not to mention its discomfort, no matter how favorable the conditions for its performance. The patients all, sooner or later, suffer from cystitis and its sequelæ.

[1] Journal of American Medical Association, April 7, 1894.
[2] Ibid., March 22-29, 1902.

4. Prostatectomy gives the best permanent result, and is fraught with very little more danger than prostatotomy.

5. Suprapubic prostatectomy should be limited to exceptional cases of enormous intravesical enlargements of the prostate. It appears to us to endanger the sphincteric control more than the perineal operation. It is more sanguinary and the work is more difficult and distant from the operator.

6. The perineal is the most direct and least bloody route. It admits of a very large opening, and permits the prostate to be drawn quite into the open before it is attacked. It gives the greatest security against injury to the bladder wall and least liability to disturbance of the internal sphincter. It endangers the rectum least and affords the best drainage.

7. It can be best performed through a Y-shaped incision, with a Sims speculum for a posterior retractor. The prostate is drawn out easily with sharp hook retractors, and best separated from the bladder from behind forward. The operation should never be performed in the dark—*i. e.*, through a small incision.

8. It should always be an intracapsular enucleation *en masse*, allowing the anterior isthmus to remain. The hæmostasis may be secured with forceps or a packing of subiodide of bismuth (not iodoform) gauze. The permanent catheter should not be introduced until the perineal drain is removed.

9. The patient should be kept in a semisitting position for seventy-two hours after the operation, and should be out of bed by the fifth day. He should drink large quantities of water from the onset.

10. Anæsthetic is *sub judice*. Phosphate of sodium should be administered to keep the urine acid, and urotropine as an antiseptic. The personal equation must never be lost sight of in operating on these cases, and attention to every small detail of the patient's general condition is necessary for the best results.

Ferguson[1] objects to the extensive incision practiced by Murphy; he asserts that by a simple linear median incision in the peritoneum, and the insertion of his special retractor into the bladder, the prostate can be brought completely under digital control, and removed either by enucleation or by morcellement. He has operated in 21 cases in this way without a death.

Albarran reported to the French Urological Congress in October, 1901, 14 cases of total removal of the prostate by perineal incision, without a death. He makes a prerectal, bi-ischial incision, hemisection of the prostate, subcapsular enucleation of the gland, and finally

[1] Journal of American Medical Association, October 25, 1902.

sutures the prostatic urethra. This operation is now the favorite with the French school.

Deffis[1] describes perineal prostatectomy as practised in Mexico, where 30 cases have been operated on in ten years, with but 2 deaths; in 7 cases practically the entire prostate was removed; several of these specimens were presented to the museum of the Necker Hospital in Paris. The operation consists simply of a perineal boutonnière, with enucleation of the prostate from its capsule.

Syms[2] reports 20 cases operated on by perineal enucleation, without a death. He endeavors to depress the prostate into the perineal wound by introducing a small rubber bag into the bladder, and then inflating it.

Fuller[3] states that he has lost but 1 of his last 18 perineal prostatectomies; but that he performs the suprapubic more frequently than the perineal operation.

It is evident that perineal prostatectomy, practised through various incisions, furnishes a mortality distinctly less than that incidental to the suprapubic operation; therefore, that it will become the operation of choice. Whether the extensive perineal incision proposed by Dittel and practised, with minor variations, by Kocher, Belfield, Albarran, Murphy, and others, will ultimately be found essential, is for the future to determine. My own practice is now a median perineal incision dividing the membranous urethra, and extended when necessary through the floor of the anterior half or more of the prostatic portion, with digital or instrumental removal of prostatic masses through this cut. If large prostatic masses projecting into the bladder are inaccessible by this avenue, suprapubic incision is made, masses removed, and the bladder sutured, with drainage below. While the choice of details must be determined by further experience, it would seem that perineal prostatectomy will become a standard operation.

Adenot[4] excised the prostate for malignant degeneration by the perineal route, using the bi-ischial incision popular with the French school. The patient recovered, though death from cachexia occurred four months later.

This operation inaugurates a new method of dealing with malignant disease of the prostate.

Andrews,[5] after reviewing the relative merits of suprapubic and perineal prostatectomy, asserts that the ideal method must leave the urinary tract unopened, and the wound therefore aseptic. He pro-

[1] Annales des mal. des org. genito-urin., October, 1902.
[2] Journal of American Medical Association, October 25, 1902.
[3] Ibid.
[4] Société de Chirurgie, October 16, 1901.
[5] Journal of American Medical Association, October 18, 1902.

poses, and in 3 instances has executed, an "infrapubic section for prostatectomy."

The considerations which led him to this method are:

1. That the prostate enlarges chiefly toward the bladder, merely because the enlargement in all other directions is prevented by firm bony or ligamentous boundaries. 2. That release of the enlarged organ from the upper restraining vicinage permits it to drop toward the rectum, and thus removes the urinary obstruction. He endeavors to secure this release of the prostate from its unyielding surroundings by dividing the levator ani fibres, the deep fascia and puboprostatic ligaments anterior to the urethra; he also excises the pre-urethral portion of the prostatic ring.

The conclusions of this ingenious study are:

1. The narrowness of the male pelvic outlet becomes surgically important with the overgrown prostate.

2. Overgrowth of prostate does not cause obstruction unless there is also outside pressure.

3. This may come from the ligaments and muscles without actual pressure of the organ against bony structures.

4. Releasing the prostate from the fixed space behind the pubes allows it to expand and cures the obstruction.

5. This can be done best by an anterior incision, and should be accompanied by a cutting of the prostatic ring and removing a segment extra-urethrally.

6. Incidentally the change of position, lowering the prostatic outlet, does away with the retroprostatic pouch and greatly assists natural drainage.

7. The separation of the prostatic and urethral ligaments from the pubes, and the weakening of the urogenital diaphragm, is not to be avoided, but sought.

THE EXTERNAL GENITALS.

Carcinoma of the Penis. Englisch[1] states that of the 540,000 patients admitted to the Vienna hospitals in 1892 to 1898 there were 12,607 cases of carcinoma; of these 81 (1.8 per cent.) developed in the penis. He collects from various sources 540 cases (including 12 personal observations); of these 49 per cent. affected the glans penis, 29 per cent. the prepuce, 13 per cent. the skin, 6 per cent. the meatus, and 3 per cent. the frenum and vicinity. Infection of the inguinal and intrapelvic lymph glands is found more frequently with carcinoma of

[1] Allgemeine Wiener med. Zeitung, 1902, No. 16.

the glans (in 79 per cent. of these) than with cancerous disease elsewhere in the penis. Englisch considers syphilis a predisposing factor; in 3 cases he has seen the direct and rapid transition of a syphilitic ulcer into carcinoma.

Wichmann[1] reports a case of primary urethral carcinoma in a woman, aged forty-three years.

Calculi in the Tunica Vaginalis. Cruchandeau[2] examined the tunica vaginalis in 57 subjects over fifty years old. In 11 calculi were found in the tunica (seventeen stones in all); in 8 subjects the stones were free within the sac, in 3 they were attached to the pedicled hyatid. He ascribes them to senile changes in the vessels.

Obstruction of Spermatic Canal. Rasumowsky[3] describes an operation for restoring the spermatic canal which has been obstructed by gonorrhœal epididymitis or other lesion. He resects the diseased epididymis and anastomoses it with the vas deferens; he has thus operated successfully on four subjects.

[1] Beiträge zür klinische Chirurgie, 1901, p. 193.
[2] Bulletin de la Soc. anat. de Paris, February, 1901.
[3] Archiv f. klin. Chirurgie, Band lxv.

DISEASES OF THE KIDNEYS.

By JOHN ROSE BRADFORD, M.D., F.R.C.P.

CLINICAL METHODS OF DETECTING THE EFFICIENCY OF THE KIDNEY.

Condition of the Kidneys. It is often a matter of extreme importance to the surgeon to determine whether the kidneys are seriously affected or not in cases where operative interference, either on the kidney or on other organs, is necessary. To the physician the question is equally important from at least three points of view: (1) To determine, in cases where urinary changes are present, whether serious organic disease is present or not; (2) to form an estimate not only as to the kind of disease present, but also as to its degree, in order to arrive at data affecting the prognosis; and (3) to differentiate, in cases where cardiac and renal symptoms are present, whether the malady is primarily renal with cardiac complications, or primarily cardiac with renal congestion. The problems presented by these conditions are always more or less obscure and difficult of interpretation. The quantity of urine, its specific gravity, the amount of albumin, the nature and character of the casts present, have each and all been used at different times as methods to arrive at the desired conclusions. They are all of value, but are liable from time to time to be misleading. In most serious organic diseases of the kidney the specific gravity of the urine is liable to be diminished, and for that reason a urine of persistently low specific gravity is always to be looked on with suspicion. Serious and even fatal Bright's disease, however, may occur, and the urine may retain a high specific gravity, as high as that seen in cases of mere passive congestion of the kidney dependent on heart disease. Thus, conclusions based on observations of the specific gravity may be erroneous.

As regards the quantity of urine secreted, there are numberless sources of error, so that conclusions based on this require to be controlled in a variety of ways. The quantity of albumin is also most misleading, as some of the most serious forms of chronic renal disease may exist and yet only produce a trace of albumin in the urine. Further, there is evidence that the granular kidney may not only exist, but may even cause death from complications, without the presence of any albuminuria.

On the other hand, large quantities of albumin may be found in the urine not only in cases of so-called cyclical or physiological albuminuria, but in forms of toxic nephritis, as, for instance, in pregnancy, and yet where, with the subsidence of the cause, the albuminuria will completely clear up without permanently or seriously damaging the kidney. For all these reasons clinicians have long sought other methods of investigating the conditions of the renal filter, and more especially by noticing the interval that elapses between the administration of a substance and its reappearance in the urine. Pugnat and Revilliod[1] give a very complete account of the various clinical methods which may be adopted in order to determine what French authors talk of as "renal permeability." They draw attention to the fact that methods of this kind were used as long ago as 1825, by Wöhler, and that it has long been noted that in certain cases of gout where the kidneys were involved the administration of such substances as asparagus and turpentine is not followed by the excretion of the characteristic odorant bodies in the urine; and in 1856, Beauvais came to the conclusion that the non-elimination of such odorant bodies in the urine was a characteristic sign of the existence of Bright's disease, and this even if albuminuria and dropsy were absent. Between that time and 1897 a number of observers showed that various medicinal substances were excreted much more slowly than normally in the urine in persons suffering from renal disease, and among these may be specially mentioned iodide of potassium. It was not until Achard and Castaigne brought forward the methylene blue method, in the year 1897, that any great attention was given to the subject. Since then Lépine has introduced the use of rosaniline for the same purpose. More recently still phloridzin has been employed with similar objects. These methods have been employed not only to determine the differences existing in the excretion of these substances in healthy kidneys and in renal disease, but also as means of differentiation to a certain extent in different forms of renal affections. In the case of methylene blue and rosaniline the problem is simply one of the excretion of a coloring-matter. Certain drugs, such as iodide of potassium and salicylate of soda, whose presence is readily revealed in the urine, may be used with more or less similar objects—merely testing the efficiency of the filter. Phloridzin, however, belongs to a totally different group of substances, inasmuch as the administration of this substance causes glycosuria, owing to a specific action on the renal cells. Pugnat and Revilliod in their paper advance the theory that the use of methylene blue, or of rosaniline, is a means of determining the state of efficiency of what they describe as the epithelial filter; and

[1] Archives Générales de Médecine, July, 1902.

that, on the other hand, salicylate of soda and iodide of potassium give information as to the degree of efficiency of the glomerular filter; and, further, that the use of phloridzin affords information as to the physiological integrity of the glandular epithelium of the kidney.

Determination of the Permeability of the Kidney. METHYLENE BLUE. One c.c. of a 5 per cent. watery solution of methylene blue is injected deeply into the muscles of the buttock. The urine is collected half an hour afterward, and then at intervals of an hour until the excretion of the blue is ended. Three observations have to be made—the time of occurrence of the excretion, the hour at which it reaches its maximum, and that at which it ceases. Most authors consider that normally the excretion begins an hour after the injection, and reaches its maximum from the third to the fourth hour, and then slowly declines, ceasing in thirty-five to seventy-two hours afterward; and, further, that the quantity of methylene blue excreted in the first twenty-four hours after the injection corresponds to at least half the quantity injected. A retarded elimination, where the methylene blue does not appear in the urine within an hour of the injection, and where the maximum occurs after the fourth hour, is a certain indication of a diminution in the renal permeability. On the other hand, it has been abundantly shown that in certain forms of renal disease, especially in chronic parenchymatous nephritis, the excretion of methylene blue may be more rapid than normal. This was first established by Bard, and the observations of the authors quoted would seem to substantiate the proposition advanced by him, that in interstitial nephritis the excretion of methylene blue is delayed, whereas in so-called parenchymatous nephritis, whether acute or chronic, it may be more rapid than normal. Under normal conditions the elimination of methylene blue is continuous, although diminishing in amount until it ceases. In disease the elimination may be intermittent or continuous and remittent, the quantities excreted undergoing increase and diminution in a more or less rhythmic fashion; and the authors have observed this type of excretion more especially in diseases of the liver, in interstitial nephritis, and in young persons affected with various neuroses. Pugnat and Revilliod conclude, as regards the excretion of methylene blue: 1. That it should take place, under normal conditions, within from half an hour to an hour after the injection; and that if it is delayed beyond this it is a certain sign of diminution of the renal permeability. 2. That the maximum excretion should take place normally from the third to the fourth hour. If it occurs before this, it points to an increase in the permeability; if later, to a diminution. 3. That normally the curve rapidly ascends, and then progressively and slowly descends. Further, that both in acute and chronic tubal nephritis the permeability of the kidney, as determined by methylene

blue, is either normal or increased. They also consider that in tubal nephritis complicated with secondary interstitial changes the elimination of methylene blue is not retarded, but it may be prolonged, and, perhaps, intermittent. Lastly, that interstitial nephritis, and in the renal cirrhosis accompanying general arterial degeneration, the methylene blue test shows that the renal permeability is diminished to a variable extent. It would seem from these results that this method is of definite value, not only from the point of view of the diagnosis of the existence of renal disease, but also as a means of differentiating different varieties of chronic renal disease. It is also of interest to observe that in such serious diseases as acute and chronic parenchymatous nephritis the efficiency of the kidney as a filter, at any rate for some substances, is not very seriously compromised.

ROSANILINE. A similar method is followed in conducting observations with rosaniline, except that 1 c.c. of a 1 per cent. solution was employed. The coloring-matter, under normal circumstances, always appears in the urine in half an hour after the injection; and the maximum is observed at the second, but more often the third, hour. In twenty-four hours the excretion is always completed, and it is most frequently over in twenty hours. Pugnat and Revilliod observed the excretion of rosaniline in some thirty cases of renal disease, and they note that its excretion is never polycyclic, as is sometimes the case with methylene blue. The rosaniline method requires a less expenditure of time than that of methylene blue, but otherwise there is not much difference in the results.

IODIDE OF POTASSIUM. The injection of iodide of potassium hypodermically has a serious drawback in that very great pain is caused. This can be reduced by injecting very small quantities, but is a very serious obstacle to the use of this method. Further, the excretion of iodide of potassium is very prolonged, and the authors conclude that the important point to determine is whether the elimination is rapid and massive, or whether, on the other hand, it has a slow and prolonged course. They consider the main point to determine is the quantity excreted in the first twenty-four hours. The method is not one that can be used in ordinary clinical investigations.

SALICYLATE OF SODA. Salicylate of soda is excreted in much the same way as iodide of potassium, and may be used instead of the latter. Under normal circumstances the salicylate appears in the urine within the first half-hour, and the maximum is seen between the first and third hours. The elimination is complete in about twelve hours. In renal affections a normal elimination occurs in tubal nephritis, and, on the other hand, the excretion is prolonged and diminished in amount in interstitial nephritis. It would seem probable that iodide of potassium

and salicylate of soda are excreted mainly by the glomeruli, whereas methylene blue and rosaniline are excreted by the tubules.

Determination of Renal Activity by Means of Phloridzin. The methods described above all deal with the efficiency of the kidney as a filter; but the renal epithelium, in all probability, has other functions, and a simple method capable of gauging the metabolic activity of this organ would be of great service, both to the physiologist and to the clinician. The synthesis of hippuric acid from benzoic acid and glycine is a chemical operation effected by the renal epithelium; and Stokvis, in 1879, made use of this synthesis in order to determine the physiological activity of the kidney. He showed that the formation of hippuric acid after the ingestion of benzoic acid was diminished in cases of parenchymatous nephritis, and that in amyloid disease of the kidney and in interstitial nephritis the diminution in the formation of hippuric acid was less than in parenchymatous nephritis. This method of gauging the activity of the kidney fell into disrepute, inasmuch as the synthesis of hippuric acid from benzoic acid can be effected by other organs than the kidney, and, therefore, the method is unreliable for this particular purpose. Further, there is no ready method for determining exactly the amount of hippuric acid present in the urine.

Achard has used phloridzin and the glycosuria produced by its action as a means of investigating the metabolic activity of the renal epithelium. There would seem to be little doubt that the glycosuria following the administration of phloridzin is of renal origin and dependent upon a specific action exerted by the renal cells under the influence of this substance. From this fact the conclusion has been drawn that the glycosuria following its administration may be used as a measure of the activity of the renal epithelium. Klemperer, in 1895, gave phloridzin by the mouth for purposes of diagnosis, and showed that in certain cases of Bright's disease glycosuria did not ensue. Levy, in 1896, showed that the subcutaneous injection of phloridzin would cause glycosuria even in cases of renal cirrhosis. The administration of this substance by the mouth is undesirable for this particular purpose, as glycosuria is not induced with absolute certainty by this method. Achard and Delamarre have shown that very small doses of 5 milligrammes may be used subcutaneously without producing any ill effects, and that this quantity will produce glycosuria in cases where the kidneys are healthy; 1 c.c. of ½ per cent. solution of phloridzin is injected deeply into the muscles. Delamarre made observations on 152 cases, and showed that in healthy subjects the sugar appears in the urine in from half an hour to one hour after the injection, and disappears in from two to four hours, and under normal circumstances the quantity of sugar excreted varies between ½ gramme and 2 grammes.

Delamarre found an excretion of sugar of this type in 62 of his cases where the patients were either healthy or did not suffer from any renal affection. In 57 cases the excretion of sugar was less than ½ gramme, and among these were 14 cases of interstitial nephritis, 6 of saturnine nephritis, and 4 of secondary ascending nephritis. The other cases were albuminuria of divers origin, such as cardiac cases and cases of pregnancy. In 23 cases Delamarre observed what he calls an exaggerated form of glycosuria, consisting either of an actual increase in the amount of sugar eliminated or a prolongation of the period of elimination. In most of these cases the patients were suffering from acute affections, such as bronchopneumonia, enteric fever, acute rheumatism, and in some instances the excretion of sugar amounted to as much as 6 grammes. Pugnat and Revilliod have carried out observations on 30 cases, for the most part patients suffering from various forms of nephritis. The main object of these authors was to investigate the question whether the glycosuria presented differences in tubal nephritis and interstitial. They determined the time of appearance of the glycosuria and its duration, and also the quantity eliminated. Their results show a considerable variability in the time of occurrence of the glycosuria. This occurred from one to three and one-half hours after the injection, and they do not consider that any conclusions can be drawn from the time of occurrence of the glycosuria, or even from its duration. On the other hand, they are inclined to think that the amount of sugar excreted may afford some valuable indication as to the nature of the renal affection. In 21 cases of renal disease tested in this manner with phloridzin there was no case of a hyperexcretion of sugar; and, further, they state that in no case was the quantity of sugar excreted normal in amount. On the other hand, in 13 cases a marked diminution was observed, and in these cases the elimination was of short duration; and in 8 cases no glycosuria occurred. They draw the conclusion that the quantity of sugar eliminated is a fact of great value, inasmuch as in healthy persons the quantity is normal, whereas in those affected with renal disease it is either diminished in amount or entirely absent. These authors point out that glycosuria of a normal character may occur in cases of albuminuria, but they do not consider that this fact impairs in any way the value of the test in cases of renal disease. In one case recorded by them the patient had suffered at a previous period from œdema and other symptoms of acute renal disease, but at the time of the observation was only suffering from albuminuria, and, notwithstanding this, the excretion of sugar after the injection of phloridzin was normal in amount. The authors consider that in all probability the albuminuria in this case was dependent on the damage inflicted by the former acute lesion, and was not dependent on a pro-

gressive and general involvement of the kidney; and they conclude that it is not surprising that the healthy portions of the kidney responded in a normal manner to the phloridzin stimulation. This point is one of considerable importance in the diagnosis of renal disease, and there can be little doubt that albuminuria is very often dependent on an old lesion of the kidney produced by some former attack of nephritis, and has a totally different significance to that of an albuminuria dependent on a recent or progressive lesion. Pugnat and Revilliod also consider the question as to whether the phloridzin glycosuria can be used as a means of differentiating between the different forms of renal disease. In 5 cases of interstitial nephritis, 4 showed a marked hypoglysuria; in the fifth glycosuria was absent. In 4 cases of acute tubal nephritis glycosuria was absent in 1 case, and in 3 hypoglysuria occurred. And, finally, in 9 cases of chronic tubal nephritis, in 5 the hypoglysuria occurred, and in 4 glycosuria was absent. Absence of glycosuria after the injection of phloridzin was also noted in a case of cystic disease of the kidneys and in a case of acute degeneration of the renal epithelium.

It would seem from these results that the phloridzin test would not afford a means of differentiating between the epithelial and interstitial affections of the kidney. It is a method which has many advantages, and is easily applied, and it affords very useful information as to the integrity of the kidney. In tubal nephritis the results obtained with methylene blue on the one hand, and phloridzin on the other, are opposite in kind, the excretion of methylene blue being more rapid than normal; the glycosuria being less than normal. In interstitial nephritis the results of these two methods are more or less similar in kind, as the excretion of the blue is delayed and diminished in amount, and the glycosuria is also diminished or absent. As these authors point out, it is important to bear in mind that in renal disease these lesions are often concurrent; and, further, that cases of tubal nephritis may apparently become complicated by secondary cirrhotic changes; and that cases of primary interstitial nephritis may ultimately also present tubal lesions. They draw the conclusion that tubal nephritis renders the kidney a leaking filter and an inefficient gland, and that in interstitial nephritis the kidney is at first an imperfect filter, and then becomes ultimately a defective gland.

FUNCTIONAL ALBUMINURIA.

Influence of Posture on Albuminuria. Notwithstanding the large amount of work that has been done with reference to this condition, there are many points of obscurity, both with reference to the diagnosis of this affection, and more especially, also, as regards its prognosis.

The diagnosis of functional albuminuria is often difficult owing to the latent character of both the symptoms and the physical signs in some forms of renal disease, and more especially, perhaps, in the true granular kidney. The difficulty with reference to the prognosis lies in the fact that different authorities hold such different views as regards the relationship, if any, existing between functional albuminuria and the possible or probable subsequent development of serious renal disease. Is functional albuminuria or is it not a predisposing cause of genuine renal disease? At different periods different criteria have been used in order to determine whether any given albuminuria was of functional or of organic origin. At one time, of course, almost all albuminuria was looked upon as significant of more or less serious renal disease, but Pavy's work especially showed the fallacy of this view, as in his account of cyclical abuminuria he showed very clearly that the albuminuria might ultimately disappear. At one time great stress was laid on the influence of posture and also the influence of diet; and an albuminuria that was greatly increased by changes of posture or by diet, or even by cold bathing, was looked upon, *ipso facto*, as of functional origin. The influence of posture and of diet, however, are both very misleading, as there can be no question that in organic albuminuria dependent on definite renal lesions, often of considerable gravity, the quantity of albumin in the urine may be notably increased by posture or by diet. In PROGRESSIVE MEDICINE for December, 1901, attention was drawn to the work of Ascher and Marklen, who showed that the albuminuria of Bright's disease and of other renal affections may be notably influenced by posture; and so much is this the case that occasionally in genuine Bright's disease and in the granular kidney no albumin may be found in the nocturnal urine. The mere fact, therefore, that albuminuria is present, or is more marked in the upright posture, or is only to be detected in the morning urine, cannot be relied upon as an absolute criterion that the albuminuria is of functional origin unless there are other signs pointing to the same conclusion. The quantity of albumin is also most misleading, because although, speaking generally, the amount present in functional albuminuria is small, this may also be the case in very serious renal disease, especially, for instance, the granular kidney. Formerly, and even by some writers at the present time, great stress was laid on the presence or absence of casts. Some authorities consider the presence of casts in the urine, even of the simple hyaline tube variety, as undoubted evidence of the existence of organic lesions; and they would remove all cases of albuminuria presenting tube casts from the category of functional albuminuria. Huger[1]

[1] Johns Hopkins Hospital Bulletin, April, 1902.

records two cases of young men, aged eighteen years, suffering from albuminuria which was apparently of the functional variety, and yet in these cases the urine not only contained tube casts, but contained them in considerable abundance. In the first case the albumin and the tube casts disappeared from the urine when the patient was placed on a milk diet and put to bed. The urine passed, however, during the daytime when he was allowed to get up, contained 2 per cent. of albumin and a number of casts of the hyaline and granular varieties. In both cases albumin was absent in the urine voided on rising; it reached its maximum about four or five hours after rising, but it did not disappear entirely unless the patient was put in a horizontal position. In neither case did food have any influence on the amount of albumin eliminated, and Huger draws attention to the fact that even a larger amount of albumin might be passed before the heaviest meal of the day than in that passed an hour after. The urine secreted thirty-five minutes after lying down showed no albumin and no casts, provided that due care had been taken to empty the bladder, so as to obtain the urine that was really secreted during the period of observation. On the other hand, albumin and casts reappeared as soon as twenty minutes after the erect posture had been assumed. Exercise did not seem to have any very great influence on the quantity of albumin, as one of the patients was made to run half a mile, and examination of the urine subsequently to this showed no increase in the amount of albumin usually present. Huger found that alterations in the relative position of the legs and body when the patient sat in a chair made no difference, albumin and casts being always present. In these two cases the point of interest is not only that casts were present, but that they were present whenever albumin was found, and in numbers proportional to the amount of albumin; and Huger states definitely that, although the casts were principally of the hyaline and small variety, granular casts were also present; and that on several occasions definite epithelial casts were found.

Neither patient gave any history of any acute specific disease liable to be followed by nephritis, nor was there anything in the past history of the patients to suggest that nephritis had occurred. In one patient optic neuritis was present in one eye, but this improved later; and Huger draws attention to the fact that Ostwalt had reported two cases of cyclical albuminuria where optic neuritis was present without any other symptoms. Pavy, in his description of cyclical albuminuria, considered that tube casts were never found, and this view has been very largely accepted; and although a number of writers have mentioned that tube casts may be present, none of them have reported their cases in such detail as these two recorded by Huger. Huger sums up our knowledge

of the condition at the present time as follows: Senator and Posner believe that albuminuria can occur physiologically. Pavy would not regard it as physiological, but would look upon this condition as a so-called functional one. Klemperer considers that all signs of Bright's disease are absent, and that functional albuminuria has no real relation with renal disease, and that the latter does not necessarily develop from the former. Lecorché and Talamon regard the condition as dependent on so-called latent nephritis, and Osler also regards the presence of albumin in the urine as indicating the presence of changes in the renal and glomerular epithelium.

Ostwalt has arrived at the following conclusions: 1. Alterations in the walls of the vessels certainly play a part, and an important one, in the production of cyclical albuminuria. 2. In one case the change in the walls preceded the albuminuria. 3. We may believe that this change in the vessels is in consequence of destructive tissue change. 4. Functional insufficiency of the vessel walls allows the albumin to pass into the urine when the renal vessels are in an unfavorable hydrostatic condition. 5. Oxalate of lime circulating in the blood may act as an irritant causing albuminuria. The view that oxalate of lime may be a causative agent in some of these cases was one which Pavy in part adopted; and Huger notes that in his cases, although he often examined for the presence of these crystals, he rarely found them.

Etiology. As regards the etiology, the condition is more often found in the male than in the female, in the proportion of 88 per cent. males to 12 per cent. females; and although it may occur at any period of life, it is most frequent in adolescence. Most authors consider that posture has more influence on the albuminuria than has diet. Herringham examined one case from this point of view very thoroughly, and found that the albuminuria increased and diminished or disappeared entirely under varying conditions of posture, but absolutely irrespective of diet. Herringham considers that the albuminuria results from an increased weight of blood pressing on the renal veins, and that therefore the condition is predisposed to by a weak circulation. Bouchard's view that the albuminuria is dependent on a toxin cannot very well be accepted in the light of the fact that the albuminuria will entirely disappear a few minutes after lying down. It is not probable that gout and rheumatism are factors of any great importance as regards etiology, but it is probable that the acute infective fevers may be followed by cyclical albuminuria, and that this condition is merely a mild degree of the true nephritis which may be the sequel of eruptive diseases. One of Huger's patients had suffered from gonorrhœa, and the other had had measles and whooping-cough in early childhood, but he saw no reason in either of his cases to attribute the albuminuria to these condi-

tions. It is also a point of some importance to which he draws attention that in one of his patients the blood pressure was low, and supported the view of those who regard the condition as dependent on low tension. In the other the pulse tension was high.

Position is undoubtedly the most important factor in influencing the albuminuria. In all the cases recorded the albumin disappears soon after the recumbent posture is assumed, and reappears on rising, no matter how the hours are changed or how long the patients lie down. Albumin does not reappear as a result of diet or exercise in the recumbent posture, but appears immediately on getting up, and increases in amount in from four to six hours, and then begins to decrease. Huger notes that in his own cases albumin appeared in the urine when the patients were carefully lifted up, and that in Pavy's cases it did not.

Prognosis. As regards prognosis, Tessier does not believe that functional albuminuria is liable to pass on into Bright's disease, and he bases this conclusion on twenty-eight cases observed by himself during a period of from nine to thirteen years. Four of these patients developed Bright's disease. But Pavy, Johnston, and many other writers have recorded cases of cyclical albuminuria that have completely recovered. Huger states that many authors, in forming their prognosis, lay stress on the following points: 1. The length of time the albumin lasts each day. 2. The length of time the albuminuria has been present. 3. The amount of albumin. 4. The presence or absence of casts.

Huger does not consider that the amount of albumin gives very reliable information. In the majority of cases from 0.1 per cent. to 0.2 per cent. is present, but he states that where the larger amount has been present there is no evidence that permanent renal mischief has developed. As regards the presence or absence of casts, it is probable that with careful centrifugalization casts will be found in many more instances than has hitherto been the case. Huger concludes that in his opinion cyclical albuminuria, like pathological albuminuria, is probably due to many causes, and that it may arise: 1. From inflammatory and degenerative changes in the renal structures, as shown by the presence of casts; and he thinks that casts will be found on careful examination much more frequently than formerly. 2. Alterations in the quality of the blood, which render its serum albumin more diffusible. 3. Alterations in the blood pressure, and especially a mechanically increased blood pressure in the renal veins. The great majority of these cases of cyclical albuminuria undoubtedly get well, but occasionally, no doubt, they may pass on into Bright's disease; and Huger thinks that continued rest in bed for a prolonged period should always be advised, because under these conditions the albuminuria disappears.

The most important conclusion arrived at in this paper is the question

of the relationship existing between the presence of casts and functional albuminuria; and if, as is probable, Huger's results be confirmed by similar investigation in other cases, the serious prognosis which is sometimes given in cases of albuminuria, owing to the presence of casts, will have to be modified. Clinicians, in forming an opinion as to whether a given albuminuria is of functional or of organic origin and dependent on renal disease, will have to fall back on other methods of investigation, and more especially on the presence or absence of changes in the vascular system, and on observations on the quantity and specific gravity of the urine.

OXALURIA.

In PROGRESSIVE MEDICINE, December, 1901, the subject of oxaluria was considered in the light of Helen Baldwin's observations, which tended to show that oxalic acid could not be looked upon as a normal product of the metabolism of the tissues, and that the oxalates of the urine were derived entirely from the food, and in certain cases from decomposition of the food owing to fermentation occurring in the stomach. Klemperer[1] records some observations on oxalic deposits in the urine. He points out the frequency with which renal calculi either consist of oxalates or contain them, and, according to him, oxalates may be present in 50 per cent. of renal calculi. Klemperer holds the opinion that oxalates may appear in traces in the urine with diets which are quite free from oxalic acid, and he states that traces of oxalates may be found in the urine of starving dogs. If the oxalates are not derived entirely from the food, their physiology and pathology would present points of considerable resemblance to that of uric acid, since it is undoubted that considerable quantities of uric acid are derived from the metabolism of the tissues. It is clear, however, that even if oxalates are not derived entirely from the food, that only minimal quantities have their origin in the metabolic changes of creatin and other substances; so that diet would still play a more important part in the treatment of oxaluria than it does even in that of the excretion of excessive quantities of uric acid. The presence of an excess of uric acid in the urine may, as is well known, be treated from two points of view: either by restricting, as far as possible, its formation, or by agents directed to increase its solubility in the urine; and Klemperer is of opinion that the treatment of oxaluria should be directed on the same lines, and that the physician should not only attempt to prevent the formation, by the administration of a suitable diet, but he should also prevent the precipitation of oxalic acid in the form of

[1] Berliner klin. Wochenschrift, December, 1901.

oxalate of lime in the urine. All soluble oxalates introduced into the blood stream are at once excreted; but it would seem from Klemperer's results that only about 15 per cent. of the soluble oxalates introduced into the stomach are excreted in the urine, the remaining 85 per cent. being apparently decomposed and excreted in other forms. The precipitation of the oxalic acid in the urine in the form of oxalate of lime is necessarily in large part determined by the quantity of lime present in the urine; and Klemperer thinks, for this reason, that milk and eggs should be avoided as far as possible, whereas, meat, fat, and most vegetables, with the exception of spinach and cabbage, may be given. Former observers have shown that the urine normally contains a sufficient quantity of calcium to precipitate all the oxalic acid present, but that this is in part prevented by the acid phosphate of soda present. In addition to this, Klemperer considers that the solubility of oxalate of lime is proportional to the quantity of magnesia present in the urine, and he suggests that in addition to the dietetic treatment it is advisable to administer sulphate of magnesia in doses of 30 grains daily.

THE PRESENCE OF TUBERCLE BACILLI IN THE URINE.

It has long been known that the urine served as a channel for the excretion of the toxic substances elaborated by microbic activity; but there have been, until recently, considerable differences of opinion as to the excretion of organisms by the kidneys unless the latter were grossly diseased. Of recent years it has, however, been established that divers micro-organisms may be found in the urine without, at any rate, gross lesions of the kidney being present. It is usual for some degree of albuminuria to exist in many of the instances where organisms are found in the urine, and what was formerly spoken of as febrile albuminuria—the albuminuria accompanying acute specific diseases of various kinds—is often present. Among the most important of the organisms that have been found in the urine, the bacillus typhosus and the bacillus coli communis may be mentioned; and, more recently, the bacillus tuberculosis. The presence of the last in the urine has, of course, been associated with the presence of renal tuberculosis for a considerable time; so much so that one of the routine methods of examination in suspected renal tuberculosis is the attempt to find the organism in the urine. Walsham,[1] in a paper on "Excretion Tuberculosis of the Kidney," deals with the question of the presence of these bacilli in the urine in cases of disseminated miliary tuberculosis; and his observations would seem to show that the bacilli may be excreted

[1] Transactions of the British Congress on Tuberculosis.

through the glomeruli, and then become arrested at some point in the course of the uriniferous tubules, most often in the medulla of the kidney, and there give rise to the formation of the tuberculous foci. Walsham is of the opinion that tubercle bacilli reaching the kidney through the renal artery become arrested either in the capillaries of the glomeruli or in a small branch of the renal artery; and he holds the opinion that, although in the majority of cases the bacilli give rise to tuberculous changes at these spots, in some cases they are excreted by the glomeruli into the uriniferous tubules.

Borrel[1] conducted a series of experiments by injecting tubercle bacilli directly into the aorta. In this way he obtained a disseminated tuberculosis in the kidney; but the tuberculous lesions were localized in the interstitial tissue, and he considered that the renal epithelium played no active part in the formation of the tubercles. Further, where the bacilli were injected directly into the aorta, although the glomeruli were frequently involved, Borrel states that he never observed the presence of bacilli in the substance of the pyramids. Thus the question is inevitably raised as to whether the presence of the organisms in the uriniferous tubules is dependent on their excretion by the glomeruli and subsequent arrest in the tubules, or whether the tubules are involved secondarily by the extension of the morbid process from a small tuberculous focus in the interstitial tissue. Walsham is of opinion that the bacilli may be found in some part of the course of the uriniferous tubules, surrounded by lymphoid accumulations, but that sometimes they are found in tubules far from any tuberculous focus, and without any tuberculous change in the neighborhood. It is clear that in the latter case they must have reached the tube either by a process of excretion or by rupture of a tuberculous focus into the uriniferous tubule. Walsham is of opinion that the latter view is in many cases very difficult to accept. He considers that he has shown the presence of tubercle bacilli in the glomeruli of the kidney without any morbid change in the vessels of the glomerulus or in the surrounding tissues; and, further, that bacilli may also be present in the uriniferous tubules under similar conditions. And he thinks, for these reasons, that the bacilli have found their entrance into the tubules during a process of excretion, and not from foci in the surrounding tissue.

Some observations of Fullerton and Hillier[2] have a bearing on the conclusions arrived at by Walsham. They examined the urine for tubercle bacilli in 18 cases of phthisis, and in all cases the urine was examined by inoculation experiments, a much more delicate test of the presence of these organisms than mere staining. In 9 among these 18

[1] Annales Pasteur, 1894.

[2] Lancet, September, 1901.

patients the urine was shown by the authors to contain tubercle bacilli, and in 6 of these cases the absence of tuberculosis in the urinary tract was shown by post-mortem examination. The presence of the tubercle bacillus in the urine of cases of phthisis, apart from the existence of renal lesions, must clearly be dependent on excretion, and would resemble the excretion of typhoid bacilli in the urine in cases of enteric fever. It is quite possible that, although the normal healthy kidney may not excrete micro-organisms introduced into the blood stream, the transitory nephritis produced apparently by the toxins of acute infections may so damage the renal filter as not only to allow albuminuria, but also to allow the excretion of micro-organisms. Further observations are needed from this point of view, inasmuch as in so many febrile diseases the kidney cannot be looked upon as perfectly normal. In tuberculosis, and especially in phthisis, quite apart from the development of local tuberculous lesions in the kidneys, these organs may be affected by waxy disease, or perhaps still more frequently by parenchymatous nephritis; and in some cases the renal lesion may be so advanced that the patient may actually come under observation on account of this rather than for the symptoms produced by the underlying malady. It is not, therefore, unreasonable to suppose that earlier and slighter lesions may be sufficient to allow of the passage into the urine of microbes. If this should be substantiated, the diagnostic significance of the presence of tubercle bacilli in the urine would not be as great as it is usually held to be unless there are other symptoms and changes in the urine pointing to the existence of a renal lesion.

GASTRIC SYMPTOMS IN FIXED DISPLACEMENTS OF THE KIDNEY.

Displacements of the kidney, whether movable or fixed, frequently give rise to symptoms requiring surgical interference, and in some of these conditions the possibility of an erroneous diagnosis is very considerable. Such errors are, on the whole, more likely to be made in cases where the displacement is a fixed one than in the ordinary form of movable kidney, inasmuch as the symptoms produced by this condition are so well known. A movable kidney may give rise to a series of symptoms referable to the stomach, or even, in some instances, to the alimentary canal; and it is generally recognized that a movable kidney may give rise to considerable gastric disturbance, owing probably to traction on the pylorus and duodenum, and in some cases this is sufficient to give rise even to jaundice. Some of the gastric attacks in movable kidney are accompanied with so much pain as to merit the term of crises, although in the case of fixed displacements of the

kidney such symptoms are usually absent, and errors are likely to be made for one or two reasons. Examination of the abdomen may reveal the presence of a tumor in an anomalous position, and this may be erroneously diagnosed as a new-growth when it is only a displaced kidney. In other instances swelling of the kidney suddenly occurs, apparently from torsion of the renal vein or from interference with the circulation through the organ; and this, being accompanied by considerable pain and tenderness, is erroneously diagnosed as inflammatory in origin, and if, as is sometimes the case, the kidney happens to occupy a position in the iliac fossa, the case may be looked upon as one of appendicitis. It is unusual for patients with a fixed displacement of the kidney to present symptoms referable to the stomach or alimentary canal, but such a case is reported by Fromant,[1] and is of considerable interest. The patient was a woman, aged forty-two years, who had suffered from a series of symptoms for the last two years which had led to the diagnosis of cancer of the stomach, owing to the fact that, along with abdominal pain, vomiting had been present, and on more than one occasion hæmatemesis had occurred. There had also been a general failure of health and considerable wasting; and a tumor in the umbilical region had been detected which, at first sight, gave the impression of being a new-growth in the omentum. The urine was normal and contained neither albumin, nor pus, nor blood. The patient gave a history that from the age of seventeen years to that of thirty-five years she had suffered from occasional intermittent pain in the abdomen which radiated into the labia, and which presented many of the characters of renal colic. Laparotomy was performed, when it was found that the kidney was in an anomalous position, being fixed above and to the right of the umbilicus. The point of interest with reference to the symptoms of the case rested in the fact that the kidney was quite fixed, and could not be moved in any direction. The wound was plugged with gauze and closed, and for two and one-half years after the operation the patient was free from all symptoms. In 1902 the patient came under observation again, and a tumor was found of the same size and in the same position as in 1899. A second laparotomy was performed and the organ removed. It was found that the kidney was fixed over the right sacro-iliac synchondrosis; that it was oval in shape and slightly anomalous in form, owing to the complete absence of the sinus. The pelvis was atrophied, but there was no hydronephrosis or pyonephrosis, and the cortical and medullary substance was quite distinct. On histological examination there was no evidence of any inflammation or of any fibrosis, but the glandular elements were generally atrophied. The

[1] Lyon Médicale, June, 1902.

point of interest about this case, apart from the original error of diagnosis, lies in the fact that the patient presented very obvious gastric symptoms, notwithstanding the fixity of the displaced kidney. The author draws attention to the fact that the absence of marked histological changes in the kidney is fairly characteristic of these ectopic kidneys; and, further, that in many cases where the organ has been quite fixed in its anomalous site the patient has presented very marked symptoms of gastric disturbance. He is inclined to think that the abdominal pain and other symptoms must be dependent on the compression of the neighboring organs, inasmuch as it is difficult to suppose, with the fixity of the kidney, that it is possible that the kidney itself should become congested as a result of torsion. Further, the case shows that any operation less radical than a nephrectomy is apparently useless for the relief of the symptoms presented by these patients. Owing to the anomalous position and fixity of the organ, abdominal nephrectomy will have to be performed in these cases, the lumbar route not being available; and it must be borne in mind that it is not unusual for the second kidney to be anomalous in some way in these cases, so that prior to the removal of the displaced organ it is desirable, if possible, to ascertain that the second kidney is actively functional.

Fixed displacements of the kidney are usually found in one of three positions, namely, over the sacro-iliac synchondrosis, in the concavity of the sacrum, or in the iliac fossa. When situated over the sacro-iliac synchondrosis the diagnosis of a growth, either gastric or omental, is most likely to be made. If situated in the concavity of the sacrum, rectal examination will often reveal the presence of what is apparently a tumor; and if in the right iliac fossa the diagnosis of appendicitis, or a typhlitic abscess, or of a growth of the cæcum, is the error most likely to be made.

MALIGNANT DISEASES OF THE KIDNEY.

Boyd and McFarlane[1] record a case of tumor of the kidney, of the variety known as hypernephroma, or tumor beginning in and having in many respects the structure of a suprarenal rest. The patient was a woman, aged thirty years, who was six months pregnant, and came under observation presenting the physical signs of a tumor in the right loin below the liver. The patient was anæmic, but was not cachectic, and the urine was normal. The tumor rapidly increased in size, so much so as at one time to lead to the suspicion that an abscess was present; and an incision was made and the existence of a growth dis-

[1] Proceedings of the Pathological Society of Philadelphia, June, 1902.

covered. At the post-mortem examination the only lesion of any interest and importance was the growth in the right kidney. The ureter and pelvis of the kidney were normal. The kidney itself was matted together to the surrounding cellular tissue, which was greatly thickened and infiltrated. On dissection it was found that the kidney itself was really free from disease, and this accounted for the fact that during life the urine had been normal. The tumor was situated at the upper part of the kidney substance, and was separated from the kidney by a band of fibrous tissue. The growth showed no disposition to infiltrate any neighboring organs, and there were no metastatic deposits; and, as mentioned above, although adherent and apparently associated with the renal substance, it was really sharply marked off from it. The tumor presented microscopically the characters which are associated with those arising from adrenal rests, and more especially the very characteristic feature that the cells of the tumor had undergone fatty degeneration. The cells of the tumor were arranged in rows and in intimate association with the capillaries, as is usually the case in these tumors; and this is what causes them to assume a superficial resemblance to normal suprarenal structure. Hypernephromata, the name now attached to the renal tumors springing from adrenal rests, are of great interest to the pathologist, to the clinician, and to the surgeon. From the pathological point of view they are of interest, as they afford an illustration of a growth having malignant characteristics which yet has a structure that closely approximates in character to that of a normal gland of the body, namely, the suprarenal; and, further, these tumors begin undoubtedly in what are known as adrenal rests, which are so commonly imbedded in small masses in the upper extremity of the kidney. These growths, at any rate in their early stages, and even sometimes when they have reached a large size, differ from some forms of malignant disease in the absence of marked infiltration and involvement of surrounding structures; in fact, they are very commonly surrounded by a fibrous capsule. Dr. A. O. J. Kelly, in a discussion on the author's case, remarked on the rarity with which hypernephromata are recorded, inasmuch as there are several reasons for thinking that ordinary carcinomata and sarcomata of the kidney are in reality in their origin adrenal tumors. The encapsulation of a tumor is also a matter of interest, as at first sight it would seem to separate these growths from other varieties of malignant disease. But this encapsulation is not seen in the more advanced stages of the growth, where the capsule may become perforated and the growth spread widely. To the pathologist, therefore, these tumors are of great interest from the point of view of the nature and etiology of malignant growths. Their origin in embryonic remains, their structure, resembling that of a normal gland,

and their encapsulation in the earlier stages of the growth, are all features of interest. In some respects these growths resemble the malignant tumors of the thyroid, which reproduce with more or less accuracy the normal structure of the thyroid not only in the primary growth, but also in the widespread secondary deposits that are so apt to occur in that disease. To the clinician the hypernephroma is of importance, inasmuch as it may produce a very large tumor having the characteristics of a renal tumor, but without any morbid change in the composition of the urine. In at least half the cases of so-called malignant disease of the kidney no urinary changes are present. If the view is correct that many forms of carcinoma and of renal sarcoma originate as hypernephroma, or are in reality hypernephroma, the absence of hæmaturia and other renal changes in so many cases of malignant tumors of the kidney is readily explained. It is possible that by paying attention to this point a diagnosis as to the nature of a renal tumor and the probability of a hypernephroma being present may be made. Further, the hypernephroma is a slow-growing tumor, and the patient may be conscious of its existence for many years. Although the absence of urinary changes is an argument in favor of a renal tumor being a hypernephroma, the presence of hæmaturia and other alterations in the composition of the urine does not exclude the existence of this form of tumor, inasmuch as perforation of the capsule may take place, and the growth may spread into the pelvis of the kidney. To the surgeon this form of renal tumor is also of importance, as in some instances it is possible to remove the tumor without removing the entire kidney, the tumor itself being shelled out, or in some instances a partial nephrectomy being performed. Dr. Kelly is of the opinion that the presence of cysts in these tumors—and they sometimes reach a large size—is dependent on a proliferation in later life of portions of renal tissue included within the misplaced adrenal rests; so that, in addition to the various points of interest mentioned above, it is possible that cyst formation, at any rate associated with tumors, may arise in this way.

CALCULOUS ANURIA AND CATHETERIZATION OF URETERS.

Calculous anuria is a subject of considerable interest to the practitioner from the difficulty that is sometimes experienced in diagnosing the seat and nature of the obstruction. Further, it is a malady that in many instances is extremely insidious in its onset and course, and the clinical symptoms presented in the condition have thrown great light on the nature of uræmia, so that from all points of view the malady is

one deserving of attention. Rafin and Verrière[1] in reporting a case of calculous anuria deal more especially with the diagnosis of the seat of the obstruction. The patient, aged sixty-six years, had had good health until fourteen years before admission, when he was said to have suffered from Bright's disease, the urine containing a small quantity of albumin, and increased arterial tension being present. Some six months before admission he had suffered from a slight attack of renal colic on the left side, and on one occasion he had had slight hæmaturia without any pain. Five days before operation the patient was seized with intense renal colic, which was not localized definitely but which lasted for some four days; and during this period the quantity of urine underwent a considerable diminution, until finally it was completely suppressed. It is remarkable that along with the suppression of the urine the pain subsided, and with the onset of complete anuria the pain disappeared entirely, although prior to this he had complained, in addition to the pain on the left side, of some discomfort on the right side. On examination of the abdomen, pressure over the left kidney gave rise to pain, and the kidney could be felt. On the right side there was no pain or tenderness on pressure. A nephrotomy was decided upon after the suppression had lasted two days, but prior to this a cystoscopical examination was made, and, thanks to this, it was ascertained that the prostate was greatly enlarged and that the orifice of the right ureter was blocked up by three calculi, lying near the ureteral opening into the bladder. Catheterization of the left ureter was at once attempted, and a sound was passed into the ureter, but was immediately arrested. Small elongated clots were seen to escape from the orifice of the left ureter. By this method it was ascertained that the anuria was dependent on an obstruction at the extremity of the left ureter, and nephrotomy on the left side was performed. The patient, however, did not survive long after the operation, owing to enfeeblement from loss of blood. On post-mortem examination the left kidney was found to be affected by Bright's disease, and that there was slight hydronephrosis. The left ureter was dilated to within a short distance of the bladder, and there it had undergone cicatricial contraction, probably from the former presence of a ureteral ulcer, and its lumen contained several small calculi. The right kidney presented much the same appearance as the left, and the right ureter, in its lower fourth, was blocked by the presence of numerous calculi.

Rafin and Verrière consider that by means of the cystoscope and ureteral catheterization it is possible to arrive at an accurate diagnosis as to the seat and nature of the obstruction in these cases; and they

[1] Lyon Médicale, September, 1901.

consider that as soon as anuria exists a cystoscopical examination of the bladder should be made in the attempt to recognize which ureter is obstructed and the nature of the obstruction. Some former writers have advised that operation should always take place in calculous anuria before the fourth day; but these authors do not consider that any delay should take place, and that prior to nephrotomy the cystoscopical examination should be made. Albarran has proposed not only to perform ureteral catheterization, but to inject hot water into the ureter, in the hope of displacing the calculus and diminishing the spasm of the ureter, and in this way overcoming the obstruction. In many cases this would be impracticable, owing to the scarring produced by ulcers of the ureter leading to cicatricial contraction, both above and below the actual site of the calculus. Rafin and Verrière consider that ureteral catheterization should always be attempted at the very onset of anuria, and that it can in no way be a harmful proceeding. If failure ensues, nephrotomy can then be performed. The case recorded by these writers also demonstrates the way in which ureteral obstructions develop in a latent and progressive fashion until the terminal effects cause death. Calculi may become arrested in some portion of the ureter and set up ulcerative changes in the mucous membrane, which may lead to cicatricial contraction, or in some cases may lead to perforation of the ureter, with the formation of a urinous abscess in the abdomen. These cases also may be latent, the patients never having suffered from renal colic of sufficient severity to cause them to seek advice, although in many such cases hæmaturia, slight in amount, has occurred. In a case seen by myself an oxalate of lime calculus was arrested at the junction of the middle and lower thirds of the ureter, and led to ulceration and perforation of the ureter, with the development of a large abscess in the left inguinal region. The only symptom this patient had ever suffered from was a slight attack of hæmaturia several years before the onset of his fatal illness. Rafin and Verrière further call attention to the very important and at the same time well known fact that if complete anuria becomes developed after an attack of renal colic the conclusion is justifiable that the patient has only one kidney actively functional. The second kidney may be absent congenitally, or, what is so often the case, it may have been rendered functionless by calculous disease, without the occurrence of any marked symptoms at any former period. Rafin,[1] in a further communication, deals with the means available for gauging the functional activity of the second kidney when it has been decided to operate on its fellow. Some observers use methylene blue to determine this question, on the

[1] Lyon Médicale, May, 1902.

grounds that if methylene blue is freely eliminated there can be no doubt that one kidney at any rate is functionally active. A more satisfactory method is to collect, if possible, the urine separately from the two kidneys. And this may be attempted in one of three ways: 1. One ureter may be compressed, so that the bladder only contains the urine of the opposite kidney. 2. Catheterization of one or both ureters may be performed, so as to collect directly the urine from the kidney. 3. The bladder may be partitioned temporarily by a suitable instrument, so as to collect separately the secretions of the two kidneys.

According to Rafin, the first method is not really practicable, and either the second or third are the only available ones in use. He himself has used catheterization of the ureters, although there are many difficulties in its operation. The third method was introduced by Neuman, improved by Harris and Downes, and used by Luys. Rafin has used the method in two cases, employing the apparatus of Downes. In one, a case of tuberculous kidney, the cystoscopical examination enabled the observation to be made that the pus came from the left ureter. The injection of methylene blue showed that this substance was freely eliminated, and when the urines were separated by partitioning the bladder the urine from the right kidney was found to be limpid and normal. A nephrectomy was performed on the left side, with happy results. In the second case, which was one of bilateral pyelonephritis, cystoscopical examination showed that purulent urine was coming from the left kidney. Injection of methylene blue revealed that the elimination of this substance was defective, as no notable excretion of the pigment occurred within twenty-four hours of the injection. When the urines were separated by partitioning the bladder, that on the left side was very purulent; that on the right purulent to a lesser degree. In this case evidence was obtained that the disease was really bilateral, and this was confirmed on post-mortem examination. Rafin draws attention to the fact that the methylene blue injection, the cystoscopical examination, and the separation of the urine in the bladder all yielded concordant results; in the one case pointing to the conclusion that a nephrectomy was advisable, and in the second case contra-indicating it. It would seem that all these methods have a sphere of usefulness in determining these questions.

Rafin[1] also draws attention to the great value of ureteral catheterization for purposes not only of diagnosis, but even of treatment; and he states that with very little practice catheterization of the ureters is a simple procedure, easier in the female than in the male. Subsequently to the introduction of the cystoscope into the bladder ureteral catheterization is

[1] Lyon Médicale, September, 1901.

not more difficult in the male than in the female. He has used this method of investigation in several cases of movable kidney, as he agrees with the conclusions of Albarran and others that the attacks of paroxysmal pain that these patients are liable to are very commonly due to slight distention of the renal pelvis with urine from kinking of the ureter; and he draws attention to the very important conclusion that in order for these paroxysms of pain to occur it is by no means necessary for any large retention to take place. At the last International Congress of Medicine in Paris, 1900, Michon and Pastau published fifteen cases of movable kidney, where they stated that retention varied only from seven to 40 c.c., and yet where severe attacks of pain were produced. This retention of urine in the renal pelvis in movable kidney is sometimes dependent on kinking of the ureter from the mobility of the kidney itself, but in other cases the actual cause is kinking of the ureter itself, or the presence of valvular folds in the mucous membrane of the ureter. Rafin used this method of catheterization of the ureter in a series of cases of movable kidney, and succeeded in satisfying himself that the flow of the urine was obstructed where the kidney was displaced, and that by manual reposition of the kidney the flow could be made normal again. The use of this method in movable kidney would seem to be, however, more of interest than of practical importance, either in diagnosis or in treatment; and the main fact of interest elicited is that these small accumulations of urine in the renal pelvis are capable of giving rise to some of the attacks of pain seen in the disorder.

NEPHRITIS.

Clubbing of the Fingers in Renal Disease. Clubbing and other alterations in the shape of the fingers are, as is well known, common in disorders of the circulation and of respiration. Chatin and Cade[1] draw attention to the occurrence of somewhat similar deformities of the fingers in a certain form of nephritis. In their paper they mention the fact that congenital heart disease and tuberculosis produce an enlargement of the ends of the fingers unaccompanied by any changes in the osseous structure; whereas in Marie's disease—the pulmonary hypertrophic osteo-arthritis—the enlargement of the finger ends is in part dependent on changes in the bony skeleton. Although this sharp line of distinction may be drawn between the extreme manifestations in these several conditions, yet the authors consider that the separation is not a real one; and all intermediate stages may be found between cases where the enlargement is limited to the soft tissues, and others where pro-

[1] Lyon Médicale, September, 1901.

found changes are present in addition in the osseous structures. Marie was of opinion that all these trophic changes in the extremities were really dependent ultimately on respiratory disturbance. Other authors have not accepted this view in its entirety, owing to the fact that these deformities have been found in cases unaccompanied by any bronchitis, pleurisy, or pneumonia. Instances apparently of hypertrophic osteo-arthritis have been found in association with dysentery, with syphilis, and with pyelonephritis. In many of these instances it might be possible to suppose that the changes were really dependent on septic absorption; but, according to Géraud, all these deformities of the extremities, whether of the type seen in phthisis or in that of hypertrophic pulmonary osteo-arthritis, are really dependent on changes in the blood and on lesions interfering with the oxygenation of the hæmoglobin of the blood. This author would associate these lesions, therefore, with interference with the hæmoglobin functions of the blood as well as with actual respiratory diseases. Chatin and Cade record the case of a man, aged thirty years, who was admitted into the hospital suffering from interstitial nephritis, and with some symptoms of uræmia of the gastro-intestinal type. The urine presented the characteristic changes seen in so-called granular kidney, being of low specific gravity, abundant, and containing a small quantity of albumin. The heart, however, did not show any signs of hypertrophy, and the lungs were healthy. The patient's hands, however, presented very characteristic changes, especially in the middle and ring fingers, less marked in the thumb and little finger, and scarcely present in the index. The enlargement of the extremities was unaccompanied by any symptoms, and there was no involvement of the articulation. Radiography showed that the apex of the terminal phalanx was considerably enlarged in the affected fingers, and covered with a new formation of osteophytes. The photograph showed an appearance resembling that produced by plunging a magnet into a mass of iron filings. This deformity of the fingers was only of recent origin, and was apparently associated with the development of the renal lesion. The authors have been able to collect only three other similar cases—two, recorded by Esbach, where clubbed fingers were associated with the presence of Bright's disease, and the other by Marfin, who, in a case of ascending pyelonephritis in a child, recorded the presence of osteo-arthropathy like that seen in pulmonary hypertrophic osteo-arthritis. In the case recorded by the authors neither the cardiac nor pulmonary organs could be held responsible for the clubbing of the fingers, and they consider it is more associated with the anæmia, which was very marked in this case.

Lesions of the Pyramidal Portion of the Kidney in Nephritis. Inflammatory affections of the kidney are usually held to affect more

especially the cortex of the organ, unless they are consecutive to lesions in the lower urinary tract. Bright's disease and other forms of nephritis are looked upon especially as diseases of the cortex of the kidney. The lesions that are found in these cases in the medulla are frequently looked upon as purely secondary and of no great practical importance. V. Babes and H. Densusianu[1] draw attention to the fact that it is by no means unusual for primary lesions to be present in the pyramids in cases of nephritis. Levaditi was apparently the first to show that lesions of the pyramids were produced directly by the action of certain toxic substances experimentally. This is especially so in the case of vinylamine, a substance which produces effects on the kidney very similar to those seen in the nephritis complicating certain acute specific diseases. So that at any rate, as regards the action of this substance, it can be definitely shown that the lesions in the collecting tubules are directly produced by the toxic agent. Babes and Densusianu hold the opinion that lesions localized in the medullary substance may be seen as a result of the nephritis complicating both scarlet fever and diphtheria, and especially as a result of the nephritis produced by streptococcal infections. The pyramidal portion of the kidney may be considerably swollen, and the apical portions of the pyramids are very commonly of a waxy appearance, and this may extend so far as to reach the base of the pyramids. In others the central portion of the pyramid may be pale and anæmic, the base and the lateral portions actively congested. Babes considers that this appearance of the pyramids is not dependent upon a simple process of accumulation of casts in the collecting tubules, but to a process of degeneration and desquamation of the epithelium of these tubules; and, further, that this is associated with an inflammatory lesion in the interstitial connective tissue. So that there is, as he says, a pyramidal nephritis which presents many analogies to that seen as a result of experimental infection. The differences in the incidence of morbid processes in the cortex and medulla of the kidneys may, in part, be dependent on the anatomical distribution of the bloodvessels of the kidney, inasmuch as the circulation in the cortical and medullary portions of the organ are, to a certain extent, distinct. All the capillaries of the cortical substance open into the interlobular veins, whereas those of the pyramids open into the venæ rectæ, which, in turn open into the interlobular veins. It is, therefore, *a priori*, possible for lesions of the venæ rectæ, for instance thrombosis, to produce congestion or even hemorrhage into the pyramids without materially affecting the cortical circulation. But, as these authors point out, the text-book descriptions of the circulation in the

[1] Archives de Médecine Experimentale, 1902, No. 4.

kidneys are a little schematic, and there are many veins from the medullary portion of the kidney which open directly into the veins around the calices; and so it is difficult to accept the view that lesions confined to the pyramids are dependent simply on thrombosis of the venæ rectæ, although it is possible that these play a part in the process. Babes and Densusianu record the details of the microscopic changes in three cases—one of hemorrhagic streptococcal infection supervening during scarlet fever; the second a staphylococcic infection as a result of a wound of the arm; and the third a case of scarlatinal nephritis supervening during the period of desquamation. The interstitial tissue of the medulla was swollen, of a glassy appearance, and contained an albuminous exudate, together with a number of more or less altered red blood corpuscles. The epithelium of the loops of Henley was swollen, and in some cases the tubules were dilated, and contained a number of red corpuscles and also leucocytes. The authors draw attention to the fact that the dilatation of the collecting tubules was often enormous, and that these tubes rarely had a normal outline. The epithelium was detached in places in masses. Elsewhere the epithelium was flattened and necrosed. Although no doubt portions of the degenerated epithelial masses seen in the collecting tubules are derived from the cortical substance, this does not account for the whole of the changes present, as, for instance, the desquamation of the epithelium. Further, the characters of the epithelial masses within the tubules are such as to show that they are derived from the medullary and not from the cortical portions of the kidney. These authors draw attention to the very important fact that the very large casts often found in the urine cannot be derived from the cortex. They conclude, therefore, that there is a true nephritis of the medulla, local in origin, and not secondary to the cortical changes. They consider that these lesions of the pyramids must play a very important part in the pathology of nephritis, inasmuch as the destruction of the tubules produced by the desquamation of their epithelium may probably be the cause of the anuria sometimes observed. In the case of scarlatinal nephritis examined by these authors the lesion supervened during the period of desquamation, and was accompanied by albuminuria and hæmaturia, followed by suppression. The vascular lesions in the kidney were very extensive, inasmuch as the venæ rectæ and the interlobular veins were in places blocked by thrombi up to their junction with the renal vein. The most extensive lesions were found in the interlobular veins, and the wall of the vessels had undergone marked changes owing to hyaline degeneration. The glomeruli were hyperæmic, and their epithelium was detached in places; and this was also the case with the epithelium of the loops of Henley. The epithelium of the collecting tubules presented the well-known change that, although the

nuclei of the cells were still present, the cells themselves had become hyaline and glass-like. The changes, in short, consisted of a venous thrombosis, and especially of the veins of the pyramids, the vessel walls were also degenerated, and the collecting tubules contained an abundant fibrinous exudation, together with a hyaline or glass-like transformation of the interstitial tissue of the kidney. The authors think, from an examination of these cases, that there is a certain independence between the cortical and medullary lesions, and that even in blood infections the lesions are not necessarily limited to the cortical substance. The old distinction that in ascending infections the lesions were mainly marked in the medullary portion of the kidney, and in blood infections in the cortex, would therefore seem to be, in part, incorrect, inasmuch as in the more violent forms of nephritis dependent on blood infections the changes in the pyramids and in the papillæ cannot be looked upon as dependent on mere accumulation of epithelial masses desquamated from other portions of the kidney. The epithelium of these tubes has undergone necrosis and desquamation, and the connective tissue is infiltrated; and the authors consider that this is a true pyramidal nephritis accompanied by proliferative interstitial nephritis, and that in some cases of acute general infections, just as after thrombosis of the veins of the kidney, the lesion may be localized in this organ at the level of the pyramids.

Scarlatinal Nephritis. Although nephritis may arise as a sequel to almost any acute febrile illness, its relationship to scarlet fever is more close than to any other acute specific disease. Baginski[1] records the results of an investigation of nearly one thousand cases of scarlet fever. He observed in all 919 cases of this disease, and found among these 88 cases of scarlatinal nephritis, which gives a percentage of a little over 9. The mortality amounted to 11, and in 18 cases he states that chronic albuminuria resulted, and of these 5 succumbed. Baginski states that the nephritis always commenced before the thirtieth day, and was never observed before the sixth. This is a point of some interest with reference to the relationship between the more severe and the more trivial forms of nephritis that occur during acute specific infections. The albuminuria that is seen during the height of scarlet fever, as it is similarly seen during the height of other acute febrile diseases, is probably often to be looked upon as a transitory nephritis, although formerly simply spoken of as a febrile albuminuria. This transitory nephritis is very different in its effects and in its importance to the severe scarlatinal nephritis occurring usually later. The transitory nephritis is not characterized by any other symptoms than

[1] Klin. Therap. Wochenschrift, 1901.

the presence of albumin in the urine; but it is probably of toxic origin, and it is possible that it may lay the foundation in some cases for future renal disease. Baginski does not consider that there is any necessary relation between the virulence and severity of the scarlet fever and the severity of the nephritis. Very severe forms of scarlet fever may be seen unaccompanied by any nephritis, and, conversely, as is well known to all practitioners, very severe nephritis may supervene as the result of extremely mild scarlet fever—in some instances so mild as almost to escape observation. Malignant scarlet fever is often fatal at a time prior to that of the usual onset of severe nephritis, and in these cases only the febrile albuminuria, or so-called transitory nephritis, is seen. Baginski does not consider that the prognosis of the renal complication depends very much on the period of its onset, but is rather to be based upon the characters of the nephritis itself; and he considers that the prognosis is unfavorable if œdema is a marked symptom, if the urine contains much altered blood pigment, and especially if uræmic symptoms are present. On the other hand, it must be admitted that cases of scarlatinal nephritis associated with marked uræmic symptoms of a very severe type do occasionally recover; and although the acute uræmia of scarlatinal nephritis is an extremely formidable condition, it is probably not so absolutely unfavorable as acute uræmia complicating old-standing chronic renal disease. Baginski does not consider that it is possible in scarlet fever to prevent the onset of severe renal complications. If these develop he thinks that the patient should be kept in bed for several weeks, at least four; and he considers, further, that for a period of six weeks the patient should be kept at rest, and as much as possible in a horizontal position after the subsidence of all the symptoms. If the albuminuria is found to persist for as long as two months it is probable that the kidneys are permanently damaged, and that a condition of chronic Bright's disease may supervene. It is probably unsafe to draw any hard-and-fast conclusion from such a short time-interval as this, as in almost all forms of nephritis cases are on record where the albumin has disappeared permanently after a very much longer time than two months. Still, in the majority of cases it is probable that the conclusion that permanent renal damage is present after the persistence of an albuminuria of some two months' duration is justified.

Nitrogenous Metabolism in Bright's Disease. Butler and French[1] have investigated very carefully the nitrogenous metabolism of a case of chronic Bright's disease during a period of forty-one days, and this investigation would seem to be not only the most prolonged, but also the

[1] Guy's Hospital Reports, vol. lvi,

most complete that has been made upon the excretion of urea and other nitrogenous constituents of the urine in this malady. The case investigated was one of subacute parenchymatous nephritis, in a boy, aged seven years, who was admitted into the hospital with cough, dropsy, and albuminuria, the illness being at the time of admission of some three months' duration, and was attributed to exposure to cold; no history of scarlet fever was obtainable. During the patient's stay in the hospital subacute uræmia was present for some time, and thus the research enabled observations to be made as to the metabolism of the body and the excretion of the urinary products during a period of fair health and during a period of subacute uræmia. During most of the time the patient was kept on a milk diet, but from time to time bread and biscuits were also given; and some observations were further made on the effect of Liebig's extract of meat. The nitrogen of the food, of the urine, and of the feces was observed daily, and great care was exercised in order to control the results as far as possible, all the ingesta being weighed or measured. The authors draw attention to the fact that it is usually stated in text-books that the excretion of urea in Bright's disease is diminished, and that this is more particularly the case during the occurrence of uræmic symptoms. Butler and French insist upon the point that the quantity of urea excreted by such a patient must necessarily be less than the normal, owing to the very great diminution in the diet; but that such patients might be expected, perhaps, to excrete as large a proportion of urea as a normal person upon the same diet. They are unable to answer this question definitely, as there are no data available for determining what the exact excretion of urea would have been in a healthy person of the same age on the same diet. An indirect method of arriving at the result is to determine what percentage of the total nitrogen present in the urine is excreted in the form of urea, and to ascertain whether this proportion is diminished in Bright's disease and in uræmia. In health the total nitrogen in the urine which is present as urea-nitrogen may vary from 67.5 per cent. to 96.4 per cent., and the authors quote observations of Hale White and Spriggs which would place the average at 87 per cent. In their own observations they observed the proportion during four periods: (1) For the whole period of the experiment; (2) for the period of uræmia; (3) for the non-uræmic period, and (4) under the influence of different diets. If the coagulable proteid be deducted from the urine, the urea-nitrogen was found in Butler and French's experiments to constitute 83.5 per cent. of the total nitrogen, the extreme daily variations being 71.8 per cent. and 94.6 per cent.; therefore the proportion of urea-nitrogen to total nitrogen was within the limits found in health. During the uræmic period the urea-nitrogen formed an average of 82 per

cent. of the urinary nitrogen after the deduction of that in the coagulable proteid. Therefore, in this patient the onset of uræmic symptoms was not accompanied by any marked relative decrease in the urea-nitrogen. And, further than that, the percentage quantity of urea actually increased during the uræmic period, inasmuch as the average for this period was 2.07 per cent., whereas for the remainder it was 1.1 per cent. The authors conclude that there was no diminution of the proportion of urea-nitrogen to the total nitrogen of the urine if the coagulable proteid be regarded as an accidental body and its nitrogen first deducted from the total. Secondly, the proportion of urea-nitrogen to total urinary nitrogen was not appreciably lower when uræmic symptoms showed themselves than at other times. The total urea-nitrogen was less during uræmia, as the food was less, while the percentage of urea in the urine rose considerably. The addition of bread, biscuits, or Liebig's extract of meat to a purely milk diet caused no alteration in the proportion of the urea-nitrogen. As regards uric acid, Butler and French found that the uric acid was not diminished out of proportion to the other urinary constituents. The variations in the ratio $\frac{\text{uric acid}}{\text{urea}}$ are not greater than those which occur in health, but the ratio $\frac{\text{uric acid}}{\text{urea}}$ became higher and much more constant with the advent of uræmic symptoms. The addition of extract of meat to the diet produced, as in health, both an actual and a relative increase in the uric acid. The authors also draw attention to the fact that the proportion of nitrogen excreted, either as urea or as uric acid, remained pretty constant through the investigation, notwithstanding the alterations in the patient's general condition and in his diet.

Their final general conclusions, which are of considerable importance, are as follows: that the proportion of nitrogen excreted as urea was not less than that found in healthy persons, if the coagulable proteid in the urine be regarded as a foreign constituent and not as a true excretory product; and this statement holds good both for the uræmic and for the non-uræmic period. During the uræmic period there was an output of nitrogen in excess of the intake; and, secondly, a high and almost constant ratio of $\frac{\text{uric acid}}{\text{urea}}$. The nitrogen present in the feces constituted a larger proportion of the nitrogen output than has been found in healthy children on a milk diet. And, finally, the loss of nitrogen by other channels than the urine and feces was not apparently greater than in health.

The two points, perhaps, of most interest determined as a result of these extended observations are that there was no evidence of any marked increased excretion of nitrogenous extractive bodies other than

urea and uric acid; and the observations do not lend support to a view that has been advanced from time to time that uræmia is associated with the presence in the blood and urine of such extractive substances. Further, these observers show definitely that during the uræmic state there may be an actually greater excretion of nitrogen than the amount taken in the food. This, of course, is dependent in part on the very great loss of appetite, and also on the vomiting that occurs, limiting the amount of proteid matter available for metabolism. In other words, the diminished excretion of urea and other nitrogenous bodies in uræmia may often be related rather to the diminished ingestion than with any incapacity on the part of the kidney to excrete; and certainly uræmia, and fatal uræmia, may occur at a time when the excretion of urine and of urea are both at a high point.

Meningitis in Bright's Disease. Uræmia is liable to be accompanied by a considerable number of inflammatory and other complications, such as pericarditis, pneumonia, peritonitis, œdema of the lungs, brain, etc. Meningitis, however, is a very rare, if not an unknown, complication of uræmia and of Bright's disease. Frerichs recorded 9 cases of meningitis among 406 cases of Bright's disease. The French authors Lecorché and Talamon, in their work on albuminuria, state that they have never seen a case. Pachymeningitis, especially pachymeningitis hæmorrhagica, has been recorded by Wagner in 3 cases of granular kidney in elderly patients, and Lecorché and Talamon have had the same experience, as they record 5 cases in very old persons, seventy-one to eighty-nine years of age. Thus meningitis in all its forms is extremely rare as a complication of Bright's disease. Thévenet[1] records the case of a woman, aged fifty-two years, who when eight years of age suffered from an attack of nephritis as a sequel of enteric fever. The albuminuria arising from this disappeared, however, in the course of six months; and from the age of nine years until her admission into the hospital at fifty-two, she had not suffered from any marked urinary symptoms. In the last few months prior to her admission some uræmic phenomena had développed, such as dyspnœa, headache, and cramps in the extremities; and the urine was found to contain a small quantity of albumin; and the heart showed signs of slight enlargement and alteration of the character of the first sound. A few days after admission she suffered from epileptiform convulsive seizures, which subsequently assumed an epileptiform character. Frontal headache became marked, and the left pupil was slightly larger than the right. The respirations became periodic, so that after fifteen to twenty regular rhythmic respirations a pause of a duration equal to two or three respiratory acts

[1] Lyon Médicale, September, 1901.

occurred. Further, the patient suffered from severe pain in the spine, especially in the sacrococcygeal region, and Kernig's sign was well established, so that if the patient were seated on the side of the bed with the knees flexed, any attempt to extend the knees was impossible on account of the very severe pain produced in the back and the sacrum. The sensation was normal, and the patellar reflexes also were normal. Flexion of the head and neck also caused very severe pain. The temperature remained subnormal, and the urine fell from the normal of 1300 c.c. to 1700 c.c. on admission, to 600 c.c. No hysterical stigmata were ever present. The patient recovered from the acute symptoms after an illness lasting nearly a month, and was discharged from the hospital some two months later. The urine then contained no albumin, and she had completely recovered from all the symptoms present during the acute illness. The author discusses at some length the interpretation of the symptoms, and more especially the question as to whether the patient really suffered from meningitis, or whether all the symptoms were to be attributed to uræmia; and especially uræmia could be answerable for the spinal pain and for the presence of Kernig's sign. Kernig's sign is supposed to be limited to cases where there is an irritation or a lesion of the meninges; and certainly the presence of this together with the inequality of the pupil, the spinal pain, and the convulsive seizures are very suggestive of the occurrence of meningitis. On the other hand, it is possible that many of these effects might be produced by an increased tension of the cerebro-spinal fluid; and the authors conclude by accepting the view that the symptoms were probably dependent on "meningism," an increased tension of the cerebro-spinal fluid, and that the sign of Kernig cannot be looked upon as pathognomonic of meningitis.

Intestinal Ulcers in Uræmia. Uræmia is often accompanied with the presence of gross lesions affecting various organs in the body; some of these gross lesions are almost invariable accompaniments of uræmia, others are only met with exceptionally, but are none the less important. In some instances the symptoms dependent on these so-called uræmic lesions may actually precede the development of the more typical uræmic symptoms. Œdema of the lungs is an invariable accompaniment of the more acute forms of uræmia, and many writers have regarded œdema of the brain as equally frequent, though modern observations have not confirmed this; and at any rate it is not so constant as pulmonary œdema. The pulmonary œdema may not only be associated with uræmia, but more especially with the dyspnœa which is such a constant symptom of this condition. Pneumonia and pericarditis are also very frequent complications of uræmia, but the pericarditis, in many instances, is of the latent type, and hence readily overlooked.

Abdominal complications in uræmia are not so frequent, although peritonitis may occur. Among the abdominal complications, so-called uræmic ulcers of the intestine are of considerable importance, not only on account of the remarkable character of the lesions, but also owing to the fact that, at any rate in a certain proportion of cases, their presence produces a more or less typical clinical picture.

Mathieu and Roux[1] give an account of such a case, together with a summary of our present knowledge of this affection. Their patient, a woman, aged twenty-two years, suffered from chronic Bright's disease, which had lasted at least three years prior to death; and uræmic symptoms, such as cramp, impairment of vision, headache, had been present for some months before the fatal illness. The urine was scanty, containing 0.3 per cent. of albumin, and hemorrhages into the mucous membrane of the mouth were present, together with a little œdema of the ankles. She came under observation suffering from severe abdominal pain and diarrhœa, and at first sight the patient presented the appearance of suffering from some form of abdominal tuberculosis, the abdominal pain being extremely severe. At the post-mortem examination, lesions of chronic Bright's disease, together with great hypertrophy of the heart, were found. The main point of interest was presented by the state of the alimentary canal, inasmuch as there were six ulcers affecting the mucous membrane of the stomach; and the mucous membrane of the small intestine, especially in its lower part, was affected by extensive ulceration along the extent of 75 cm. from the ileocæcal valve upward. In places the ulcers were cleanly cut, but in others the mucous membrane was covered by extensive diphtheritic exudation. The peritoneal surface of the bowel was congested, and its surface of a dark violet color. The abdominal glands were not enlarged. The large intestine was, unfortunately, not examined, but externally presented no signs of disease. The authors, in addition to describing in detail the morbid anatomy of their case, collected from medical literature 22 similar cases, from which they deduce the following conclusions: The age of the patients was noted in 20 out of the 22 cases. In 7 cases the patients' ages varied from thirty-two to forty-seven years. In 1 case the patient was fourteen years of age, and in the remaining 12 the age varied from eighteen to twenty-four years. Thus in 13 the age at death was under twenty-four. Among these 13 cases, in 10 the small intestine was affected by very extensive areas of ulceration, especially marked in the ileum. In 1 case there was an ulcer of the stomach, and in 2 cases more or less extensive ulcers in the large intestine. In the 7 patients whose ages varied from thirty-two to forty-

[1] Archives Générales de Médecine, January, 1902.

seven, in no case were there any ulcers of the small intestine. In 3 there were hemorrhagic erosions of the stomach, and in 4 ulcers of the small intestine in small numbers. The authors, therefore, draw the conclusion that these uræmic ulcers of the small intestine are only seen in the case of young persons suffering from Bright's disease. The renal affection, which is always very advanced, reveals itself by obvious symptoms, such as anasarca, dyspnœa, headache, giddiness, epileptiform seizures, coma, and amaurosis. They draw attention to the fact that there is only one case, recorded by Dickinson, where the sole symptom observed was the impairment of vision. The urine is always highly albuminous. In all these 22 cases the involvement of the intestine was shown by symptoms present during life. In most instances a severe and persistent diarrhœa is present, and in some instances this has been quite dysenteric in its characters, especially when the large intestine was observed. In exceptional instances constipation has been noted, and this was the case in the author's patient and in the case recorded by Dickinson.

Abdominal pain of a severe type is rare, and is never observed unless the peritoneum is involved. In some instances peritonitis dependent on perforation has been present. Dickinson, in one of his cases, has recorded the existence of severe abdominal pain of an intermittent character referred to the umbilicus, and without the presence of any peritonitis. Vomiting may occasionally be present, but is more often dependent on the renal disease than upon the intestinal complication, and vomiting has been absent in more than one instance where extensive ulcers of the mucous membrane of the stomach have been present. The course of the disease in cases where these ulcers are present is generally very rapid, death occurring usually very soon after the first occurrence of symptoms pointing to the existence of the intestinal disease. In the majority of instances life has not been prolonged longer than from two to four weeks after the onset of the abdominal symptoms. But there are two cases on record where diarrhœa was present for as long as four and six months. Although the gravity of these intestinal ulcerations is very great, they are probably not invariably fatal, inasmuch as several writers, for instance Treitz and Bartels, have both, in cases of uræmic ulcers of the small intestines, observed the occurrence of healing, and even the formation of an intestinal stricture. Hemorrhage is very rare in uræmic ulcers, and was only observed four times in the 22 cases dealt with by the authors; and in those cases streaks of blood only were observed. Mathieu and Roux sum up the clinical side of this affection by stating that these ulcers occur most usually in patients suffering from Bright's disease of from eighteen to twenty years of age; they occur usually at a time when uræmic symp-

toms are present, and they reveal their presence by a persistent and intense diarrhœa, constipation and intestinal hemorrhage both being rare. Abdominal pain is not usually present, unless there is coexisting peritonitis. The duration of the illness is usually short, and the prognosis very grave, although not abslutely fatal.

The authors draw attention to the interesting fact that it is rare for both the large and the small intestine to be affected in the same patient; and that many writers have pointed out that where the large intestine was extensively involved the small intestine was intact. The involvement of one part of the alimentary tract and not the other is not, however, constant, and a few cases have been described where one or more ulcers have been found in the small intestine, together with large numbers in the large. In many cases the ulcers in the large intestine are superficial, and do not go deeper than the muscularis mucosæ. In the small intestine the ileum is the part most often involved, and the ulcers extend along the free border of the intestine, and do not specially involve Peyer's patches. Their depth is very variable, and may extend to the muscular coat or to the peritoneum, or perforation may take place. It is very common for extensive sloughs to be present, and for the margins of the ulcers to be greatly thickened. In the case of the stomach, hemorrhagic erosions are perhaps most commonly present, but ulceration of the mucous membrane of the stomach, of very varying extent and depth, may be present. The remarkable point is that the usual symptoms of ulcer of the stomach are absent, and that the progress of the ulcer is very much more rapid in these cases of uræmia.

The mechanism of the production of these ulcers is obscure, but these authors would seem to hold the view that they are largely produced by a necrosis, and that this necrosis owes its origin to the presence of toxic bodies, and possibly to the excretion by the mucous membrane of toxic substances produced by the uræmic state.

Interstitial Nephritis. Relation to Arterial Sclerosis. Bouveret[1] discusses in this paper not only the prognosis of interstitial nephritis, but also the varieties of this malady and its relationship to arterial sclerosis. He draws attention to the well-known point that the bulk of the cases of arterial sclerosis, especially in its early stages, are seen in private practice. Such patients do not seek admission to hospitals until the malady is far advanced and incurable. Bouveret apparently considers that arterial sclerosis is a misnomer, and that this disease is never primary; and he holds the view, advanced at first by Traube, that the hypertrophy of the heart and the degeneration of the arteries are always secondary to an involvement of the kidney.

[1] Lyon Médicale, October, 1901.

Hypertrophy of the heart, sclerosis of the arteries, and interstitial nephritis are all links in the same pathological chain. He points out that an obstacle to the excretion of urine, provided the urine remains aseptic and the cause is a slowly acting one, produces an interstitial nephritis; and that in course of time this nephritis is followed by hypertrophy of the heart and degeneration of the arteries, unless the patient's age or general nutrition is such as to have produced such a degree of feebleness as to prevent this reaction. In confirmation of his views as to the primary renal origin of arterial sclerosis, Bouveret draws attention to the well-known fact that hypertrophy of the heart is not uncommonly absent in cases of general atheroma, even when it occurs in young persons and in those in whom the general health is still good, and the state of nutrition such that hypertrophy of the heart might be expected to develop. Bouveret considers that the renal changes are not secondary to those of the general arterial lesions, owing to the difficulty of accounting for the fact that these lesions are so marked in the kidney, and that similar lesions in the muscular system and in other organs—liver, spleen, brain, etc.—are, comparatively speaking, rare. He also thinks that if the renal lesion were secondary to the arterial, and not primary, that unilateral renal cirrhosis would sometimes be seen; and he asks the question why, if it is not primarily renal, is the lesion always bilateral? It is obvious that if the disease is primarily renal this fact affords a ready explanation of the bilaterality of the affection. Bouveret considers that the reason cirrhosis of the kidney produces general arterial changes is that the kidney is the principal organ for regulating arterial tension, quite apart from its action as an excretory organ.

Varieties of Interstitial Nephritis. He considers that five different varieties of interstitial nephritis may be recognized: (1) The so-called aplastic form, associated with a general aplasia of the vascular system; (2) a toxic form, of which the best known type is that produced by lead; (3) that dependent on acute infections, and here the origin of the malady is often very obscure, and depends very often on acute infective diseases that have occurred in childhood or infancy; (4) the variety due to ascending infection, and dependent on some impediment to the urinary excretion, such as prostatic disease and stricture; and, lastly, the form of renal cirrhosis called by him "nephrite uricémique," and dependent on or associated with the prolonged excretion of increased quantities of the normal urinary constituents. Uric acid represents the type, according to Bouveret, of the excrementitious substances that are answerable for the production of this form of renal disease. Bouveret considers that this form of the disease is seen especially in middle-aged men leading a more or less sedentary life and living too freely both as regards the amount of fluid taken and solid

food consumed. He considers that the pathology of this form of interstitial nephritis is dependent on an overaction of the kidney stimulated to excrete by an excess of urinary constituents. In some cases this only leads to irritation of the bladder or of the ureter; but in others it causes irritation of the kidney, shown probably by congestion, and this long-continued chronic congestion terminates in sclerosis and atrophy.

Prognosis. In discussing the prognosis of the disease, it is only this last form of renal cirrhosis that Bouveret considers, and more especially for the reason that this form is extremely common in private practice, and it may not uncommonly be watched from its onset. The other four varieties of renal cirrhosis are not usually seen until the lesions have advanced to a marked extent, and a fatal termination is practically certain, although, may be, distant.

Symptoms of Interstitial Nephritis. Bouveret divides the cases of interstitial nephritis associated with an excess of uric acid into three groups: the first consisting of those where the disease is in such an early stage that, according to him, complete recovery may ensue; secondly, those in which the affection is uniformly progressive and fatal; and thirdly, those in which the course of the disease becomes arrested, but leaves incurable lesions of the heart, kidneys, and arteries. Bouveret lays great stress on the recognition of the cases falling into the first group, although he admits that such cases are not very numerous. He considers that, notwithstanding this, it is possible to assert that arterial sclerosis is curable in its early stages. The importance of this, seeing the gravity of the disease in its ordinary forms, is obviously very great; but at the same time the difficulty of recognizing with any degree of certainty the symptoms presented by such cases must cause a little hesitation in accepting Bouveret's conclusions. He points out that the symptoms of this condition, as he recognizes it, are not well marked, and the patients themselves are not usually aware of any marked impairment of health. And Bouveret draws attention to the very important point that very commonly it is only by accident that the malady is recognized, the patient frequently undergoing a medical examination for reasons other than the relief of symptoms produced by the disorder. That, however, is true not only of this early stage of arterial sclerosis, but is more or less the case in almost all forms of arterial sclerosis and granular kidney. It is by no means uncommon for these maladies to exist in a relatively advanced form without the patient suffering from any marked symptoms drawing attention to the serious underlying disease. It is not uncommon for advanced granular kidney to be discovered more or less accidentally in persons not showing any grave disturbances of health, even at a time when the duration of

life may perhaps be measured only by days or weeks. Certainly, the latency of symptoms is not a point of absolute distinction between the early stages and the advanced stages, or between the severe and the slight forms of granular kidney. Bouveret considers that the earliest symptoms produced by this slighter form of interstitial cirrhosis are especially a slight dyspnœa observable during exercise, and especially during any increased effort, such as going up stairs; palpitation, moderate in amount, sometimes spontaneous, but more often caused by exertion; an increased frequency of micturition in a patient still in the prime of life and especially to be observed during the night. In addition to these symptoms, cough is very often present, dependent on or associated with a chronic pharyngitis; and Bouveret draws attention to the somewhat important point that in many cases these patients seek advice on account of the cough, and with the idea that they are suffering from a slight form of bronchitis or asthma. At the time when these comparatively trivial symptoms are present the patient has the appearance of good health, has a good color; very commonly his state of nutrition is good, or there may be even an inclination to stoutness. Bouveret draws attention to the fact that in this early period the renal symptoms are very slight; and he lays stress on the fact that even in the early stages of interstitial nephritis the initial symptoms are not renal but cardiac, and, to a certain extent, respiratory. He considers that the absence of marked symptoms implicating the kidney is the reason why so many authorities consider that interstitial nephritis is sometimes secondary to arterial sclerosis. Bouveret lays great stress on the characters of the pulse in the diagnosis of the initial stages of renal cirrhosis; and he considers that it presents two fundamental abnormal characters; in the first place, it is more frequent than normal, even during rest, so that it may amount to between 80 and 100 even during complete rest; secondly, the tension is increased, and the vessel remains obviously full in diastole, so that considerable pressure is required to obliterate the artery, both during systole and diastole. The examination of the pulse should be made under divers conditions; for instance, during rest, after exercise, and after meals. Bouveret goes so far as to assert that the combination of increased frequency with increased tension is not only a sign of the very first importance in the diagnosis, but he considers that this association is not found in any other disease than in interstitial nephritis. Under normal circumstances Bouveret considers that the pulsation of the axillary artery cannot be felt by the finger placed between the deltoid and the pectoral, just below the clavicle, but that in the early stages of interstitial nephritis the pulsation is readily felt in this situation. In this early stage of the malady the only cardiac physical signs are that the impulse is stronger than normal,

and that the sounds are more accentuated; and this especially is the case with the aortic second sound. Auscultation of the lungs very commonly reveals nothing, but in other instances a few fine râles are to be heard at the bases. Bouveret again draws attention to the contrast existing between the negative examination of the lungs and the presence of dyspnœa produced by exertion.

Urinary Changes. The urine is a little more abundant than normal; the specific gravity is normal, or may even be, according to Bouveret, slightly raised. The density of color is not modified, in some instances the urine may be somewhat greenish. Albumin is usually absent, but traces may be present after fatigue. Many of the symptoms are aggravated after the heaviest meal of the day, and Bouveret thinks this is dependent on the absorption of fluid still further increasing the blood pressure. He draws attention to the fact that the presence of discomfort after meals, such as headache, oppression, sleepiness, and dyspnœa on exertion, may lead to an error of diagnosis, in that the symptoms may be supposed to be of gastric origin, and the patient be treated for dyspepsia. Bouveret considers that at this period of the disease it is probable that the only lesion present in the kidney is congestion. He does not consider that any more serious change has occurred than this, inasmuch as complete recovery from all these symptoms is possible. He thinks that the overgrowth of fibrous tissue in the kidney is entirely secondary to congestion, and that it is reasonable to suppose that the overaction of the gland should be accompanied by congestion. Further, he thinks that in the initial stages the high tension is also of functional origin, and that it is only later that the degenerative changes occur in the vessels. Notwithstanding the discordant results of different observers, Bouveret considers that in the earlier stages of the malady the muscular coat of the arteries undergoes hypertrophy, and that the hypertrophy of the heart is in no way special, but only part and parcel of a general hypertrophy affecting the whole arterial system. He states that he has never seen in other forms of arterial degeneration such a degree of hypertrophy of the muscular coat of the arteries as in the form associated with interstitial nephritis; and he sees in this another argument in favor of the well-known theory of Traube. Bouveret admits that the symptoms which he describes as characteristic of the initial period of the disease are slight, and to a certain extent equivocal, but he is convinced of their accuracy owing to the fact that in several instances he has seen these symptoms progress until the usual and definite clinical picture of interstitial nephritis was established.

Bouveret's paper is of considerable interest; and although the reality of the clinical picture that he draws must be admitted, the difficulty that presents itself is to feel certain that the symptoms are not

dependent entirely on vasomotor and vascular lesions; in other words, there is no unequivocal evidence that the kidneys are actually involved in this type of case. On the other hand, as mentioned above, there can be no question that the disease may advance to a high degree in the kidneys with or without the association of marked cardiac and vascular changes, and yet with the production of few symptoms. Every physician knows of cases of granular kidney where the patient has died suddenly of cerebral hemorrhage at the time when the general health was apparently good; and at the same time it must be admitted that this complication is extraordinarily apt to occur where the renal lesions are not necessarily greatly advanced.

The great value of Bouveret's paper lies in the drawing of the attention of practitioners to the importance of suspecting the existence of interstitial nephritis in cases where the patient presents no marked urinary symptoms, but comes under observation with respiratory, cardiac, or gastric disturbance.

Cardiac Hypertrophy in Renal Disease. Although the relation of cardiac hypertrophy to renal disease is a thoroughly well-established one, the mechanism of its production is by no means clear, notwithstanding the very large amount of work that has been done, especially from the pathological side, in investigating this problem. Cardiac hypertrophy is especially marked in certain forms of Bright's disease and in the granular or cirrhotic kidney; but it is by no means either an invariable accompaniment of these lesions; nor, on the other hand, is it always absent in other forms of renal disease. Even in the granular kidney, where cardiac hypertrophy is such a characteristic feature, it is occasionally absent, even when the renal lesion has advanced to a high degree. Some authors have thought that this absence of cardiac hypertrophy is to be accounted for in many cases by the impaired general nutrition or the cachectic condition of the person at the time of the development of the renal lesion. It is unquestionable, however, that extreme forms of cirrhotic kidney, and even of chronic Bright's disease, may occur even in young persons without the development of any notable degree of cardiac hypertrophy. At one time cardiac hypertrophy was associated in its development with a destruction of large areas of kidney substance; and this theory gave a ready explanation of the occurrence of cardiac hypertrophy in granular kidney. Further observation has shown that other destructive diseases of the kidney may advance to a high degree without the development of any cardiac hypertrophy. This is notably the case, for instance, in some forms of general cystic disease and in cases of congenital bilateral hydronephrosis. In general cystic disease cardiac hypertrophy may certainly be absent, and where it is present, as is sometimes the case, the kidney

substance remaining and forming the septa between the cysts has very often undergone a cirrhotic change. So it would seem that in the cystic kidney the occurrence of cardiac hypertrophy may be associated with the development of renal cirrhosis in the remaining kidney substance. In double hydronephrosis cardiac and vascular changes are also sometimes present, but in many of these it is probable that their occurrence is dependent upon some associated morbid process.

Bryant and Hale White[1] describe a case of remarkable double hydronephrosis in an infant, aged six months, in which there was extensive calcification of the arteries and obliterative endarteritis, the latter lesion advancing to such a degree as to cause death from gangrene of the foot. The double hydronephrosis was associated with hypertrophy of the bladder and the presence of phimosis, the remaining renal tissue showed an increase in the interstitial tissue. The association of the vascular lesions with the double hydronephrosis was probably accidental, and it is quite possible that it was really due to syphilis. The mere diminution in the amount of available kidney substance, whether produced by disease or experimentally by removal of large quantities of the kidney, has not, in the hands of most observers, been followed by the development of any obvious degree of cardiac hypertrophy; and it would seem as if the occurrence of this in Bright's disease and granular kidney must be dependent on some other cause. Mayet[2] brings forward some experimental evidence tending to show that the production of nephritis experimentally may be followed by the development of an appreciable amount of cardiac hypertrophy. Mayet injected subcutaneously quantities varying from 1 to 5 milligrammes of cantharidine dissolved in oil, and he obtained, both in rabbits and in dogs, albuminuria as a result. He draws attention to the fact that this albuminuria was never very persistent, nor even proportional to the quantity of cantharidine injected. The injection of 1½ milligrammes of cantharidine into rabbits caused, on the following day, a slight albuminuria, which increased in amount as the result of a second and a third injection. The day after the third injection the albuminuria disappeared, and did not recur as a result of a fourth and fifth injection. Death occurred some six months afterward, and evidence of nephritis was present, in addition to lesions in other parts, especially a myelitis. The left side of the heart was hypertrophied to such an extent as to have increased the thickness of the ventricular wall to double the normal. Mayet repeated this experiment in another instance, and obtained somewhat similar results; and it would seem that the nephritis, and possibly the other effects produced by cantharidine are capable of causing a definite hyper-

[1] Guy's Hospital Reports, 1901.

[2] Lyon Médicale, January, 1902.

trophy of the left ventricle, which is fairly rapid in its course. Clinically, cardiac hypertrophy to an extent sufficient to reveal itself on physical examinaton may be developed in as short a time as six weeks to two months from the onset of an acute nephritis. Mayet draws attention to the fact that none of the existing theories regarding the mode of production of cardiac hypertrophy are entirely satisfactory. Bright looked upon the hypertrophy and the increased tension in the arterial system as produced by the action of toxic substances retained in the blood directly on the heart; in other words, that the cardiac hypertrophy was really primary, and not brought about as a sequel to increased arterial tension. Mayet considers the clinical observation that the increase of arterial tension and the development of cardiac hypertrophy generally occur at the commencement of renal diseases as an objection to this view, inasmuch as at this stage of the disease there is no very deficient excretion of toxic substances. According to Huchard, the action of the toxic substances present in the blood would be a direct one on the endothelium of the arteries; and he apparently considers that this lesion may be developed at an extremely early stage, and before the renal changes have advanced to any high degree. These views, and especially the one advanced by Bright, possess a high degree of probability, but they lack the demonstration of the existence of these toxic substances and of their action. It has been shown that urea is capable of increasing the force of the heart-beat, and thereby increasing arterial tension; and the quantities of urea present in the blood in renal disease, even in its acute forms, are often very considerable. But it cannot be said to be clearly established that the cardiac hypertrophy or the increased arterial tension are really dependent on the presence of the increased quantities of this substance. Mayet draws attention, with reference to Traube's theory, to the fact that however important the kidneys may be, their vascular area only constitutes a very small portion of the total arterial system. He does not consider that any alteration in the calibre of these vessels is capable of producing any marked degree of tension. Most of the experiments that have been done from this point of view have consisted of ligaturing or occluding the renal artery itself; but it must be borne in mind that constriction of the branches of the renal artery will produce far greater passive effects on the circulation than will mere occlusion of the trunk of the main vessel. Mayet, however, considers that the effects produced on the arterial system in renal disease are so great that they cannot be brought about by any change of the vascular area of the kidneys themselves, and that they must be dependent on reflex effects produced on the circulation, the stimuli causing these arising in the kidneys themselves. A large number of observations have shown that stimulation

of the afferent nerves of the kidney is capable of producing very marked effects indeed on the general blood pressure; in fact, there are few nerves in the body the excitation of which produces as great effects as those seen experimentally to follow stimulation of the central end of the afferent renal nerves. Mayet would consider, therefore, that in nephritis the toxic agent causing the disease acts on the kidney structures, and in that way produces afferent stimuli which lead to a great increase in arterial tension as a result of vasoconstriction; and that the cardiac hypertrophy is developed in response to this. This theory undoubtedly has some facts in its favor, although the experiments with cantharidine, on which Mayet bases it, are by no means conclusive. It is quite possible that the action of such a toxic substance as cantharidine produces widespread effects on the arterial system not limited to those seen in the kidney, and that the cardiac hypertrophy is developed really in response to this rather than in response to the purely renal lesions. Toxic substances, as, for instance, lead or alcohol, and no doubt many others, may give rise to widespread arterial lesions in the human subject, associated with marked cardiac hypertrophy, without any well-developed lesions being present in the kidney. And, on the other hand, other toxic agents, or perhaps under certain conditions the same toxic agents, may produce very advanced renal lesions sufficient to cause death from uræmia without the simultaneous production of the usual cardiac and vascular effects. This is really the difficulty in the way of all explanations as to the actual relationship existing between renal disease and cardiovascular changes; and it cannot be said at the present time that any satisfactory explanation of this anomaly exists.

Arterial Lesions in Chronic Renal Disease. Herringham[1] has conducted a series of observations on the histological changes in the arteries of the cortex of the kidney in chronic renal disease. The observations were of a laborious character, and were conducted in 34 cases; and, owing to the large number of measurements made, were limited to the changes occurring in the cortical vessels. The relationship between arterial lesions and Bright's disease is one of great practical importance, quite apart from its theoretical interest, inasmuch as the arterial changes in accessible arteries, such as those of the wrist or of the fundus oculi, may often afford evidence as to the existence or not of serious renal mischief. Further, one of the most formidable complications of chronic renal disease—namely, cerebral hemorrhage—depends on the arterial lesions so often associated with the disease. And, lastly, the cardiac hypertrophy of renal disease is intimately associated with the arterial lesions. It is very remarkable, considering

[1] Transactions of the Pathological Society, vol. lii., 1901.

the importance of the subject and the very large amount of work that has been done on it, that there should still be the great differences of opinion that there are as to the actual condition of the vessels, not only of the kidney but of the body at large in Bright's disease and in other chronic affections of the kidneys. Herringham sums up in his paper the views of most workers on the subject. George Johnson considered that a true hypertrophy of the arterioles was present. Gull and Sutton stated that the intima was thickened, and that the muscular coat was thicker than normal, but that the nuclei were indistinct, and that the fibrous coat was not only thickened but that its tissue was hyaline and more fibrous than normal. Wilks and Moxon did not consider that there were any great changes in the fibrous coat. Thoma considered the chief lesion to be that of endarteritis. Ewald and Leyden did not observe any hypertrophy of the muscular coat, and did not confirm Gull and Sutton's observations as to the existence of peri-arteritis. On the other hand, they found that the intima had undergone hyaline changes in the case of the smaller vessels, and in the larger ones that the intima had become fibrous. Councilman[1] more recently, in 1891, states that the muscular coat of the smaller arterioles is thickened by the deposit of homogeneous hyaline material, and that the muscular fibres of the media are atrophic. Herringham considers that the discrepancies between these different observers are dependent mainly on the unreliable microscopic preparations of the older observers and on the fact that the vessels of the normal kidneys are not sufficiently carefully examined; and, further, that the observations on the pathological changes have not been controlled by actually measuring the degrees of the changes in the vessel walls. Herringham considers that in the normal kidney the intertubular connective tissue is continuous with the fibrous meshwork between the muscular fibres of the interlobular arteries and with the intertubular septa of connective tissue of the kidney. Its limits are, therefore, very inexact, and he has not been able to satisfy himself by exact measurements of its thickness in health. In disease it is certainly increased as a part of a general renal fibrosis, both around the interlobular arteries and in wedges passing in from the capsule. He considers that this fibrous overgrowth starts around or in the lymphatic channel that exists beside the bloodvessel. In many cases it only, apparently, involves one portion of the circumference of an artery, and this is the case even where the vessels are very small. Further, Herringham has never seen this peri-arterial fibrosis in chronic Bright's disease except as part and parcel of a general fibrosis; and he thinks its amount varies with this rather than with the condition of the

[1] Transactions of the Association of American Physicians.

arterial walls. For these reasons he does not believe it to be an arterial change, but rather that it is part of a general fibrosis of the kidney; and he would, therefore, "deny the existence in the kidney of any special condition deserving the name of peri-arteritis."

Herringham has examined the condition of the media in longitudinal and in transverse sections, and in this way has arrived at an estimate by measurement of its thickness. But, as he points out, measurements alone would give erroneous information, since it might be found of normal, or even of excessive, thickness, and yet the substance, instead of being normal muscle, might have undergone inflammatory or other changes. He, therefore, considers it essential to have some test of the condition of the muscle cells themselves. In order to obtain a standard of the condition of the muscle cells, he relied upon the character of their nuclei rather than upon the appearances of the muscular fibres themselves, holding the view that the loss of the staining reaction of the nuclei might be considered as evidence of pathological changes in the muscle cells. The measurements and the counts of the nuclei were made in longitudinal sections of the arteries, which were obtained by cutting sections of the cortex at right angles to the plane of the capsule. He considers, in a normal vessel, that for every 100 μ of media measured lengthwise there will be 2 nuclei for each μ of breadth, and that in health the variations from the average are not great. He states that among the 34 cases of chronic Bright's disease observed by him in no single case of the series was any true thickening of the muscular coat observed, either by cross measurement or any increase in nucleation by long measurement. On the other hand, it was very common for the media to be thinner than normal and to have fewer nuclei for a given area than is the case in health. Further, fibroid changes in the muscular coat were not infrequently seen. Under normal circumstances the interstitial tissue between the muscular fibres is just visible; in disease it is obviously greatly thickened. He further states that he has not seen in the interlobular arteries the larger patches of fibrous tissue which are not uncommonly seen in renal disease and in other conditions in the radial artery. As regards the intima, this, in normal vessels, consists of a single wavy elastic membrane lined by a single layer of endothelium. In renal disease profound changes are seen in the intima, so that instead of a single bright, wavy line inside the media there are several such, and between these layers cells are seen in scanty numbers. Herringham considers this arises from the splitting of the original elastic membrane, rather than as a result of proliferation of subendothelial cells. Herringham thinks that the elastica first swells and then divides, inclosing a hyaline mass, so that on the outer border of this a thin and imperfect layer of elastica can be traced, and

another similar layer on its inner border. This change is especially seen in the smaller arteries. Herringham has been unable to associate particular changes in the arteries with particular lesions of the renal tissue, and he states what would probably be generally accepted now, that one is not necessarily a cause of the other, as is shown by the fact quoted by him, and illustrated by some of his cases, that fibrous kidneys may occur in young persons which show no marked arterial lesions, and that in other cases where the renal arterioles are markedly diseased the renal tissue shows no profound changes. He also considers that the cardiac hypertrophy depends more upon the degeneration and rigidity of the aorta and large vessels than upon the lesion in the kidneys themselves. The changes in the large vessels greatly impair their elastic sufficiency. He regards the high-pressure pulse in the radial artery as "not due to any increased resistance beyond it, but to the removal of the elastic buffer which the aorta in health provides." The general conclusions, as a result of his observations, are: 1. That arterial lesions occur chiefly in persons over forty years of age. 2. That they bear no relation to the degree of parenchymatous disease. 3. That though they usually occur in fibrous kidneys, advanced fibrosis may be present without them. 4. That they may be independent of any renal disease at all. 5. That the changes in the middle coat of the renal arterioles are never hypertrophic in character, but atrophic and degenerative. 6. That the changes in the inner coat are, hyaline swelling in the smaller, lamination and cellular infiltration in the larger vessels, with, more rarely, a proliferation of the endothelium, or in the situation of this. 7. That cardiac hypertrophy usually occurs with these arterial lesions in the kidney, but there are so many exceptions that the latter cannot be said to be a sufficient cause of the former.

PHYSIOLOGY.

By ALBERT P. BRUBAKER, M.D.

THE PHYSIOLOGICAL EFFECTS OF IONS.

It is something new to have to turn to America for the most interesting work on any purely scientific subject, yet in physiology this has been true the past three or four years. The work begun by Loeb, about five years ago, has been continued by his pupils and assistants, as well as by others throughout the country, and to-day occupies the centre of the stage, especially in the popular mind. The problems of life, its beginning, its prolongation, and the essential nature of its processes, have always been of the most absorbing interest. Loeb's experiments and those of his confrères and pupils seem to be bringing us a little nearer the actual explanation of these phenomena. The goal is still at a distance, and many things will have to be explained before we can come to a full realization of even the present conclusions; for instance, it is evident that we will first have to learn and understand more about electricity and electrical phenomena before we can at all grasp the varied influences of kations and anions. That Loeb's and Matthews' broad generalizations exploited in the popular magazines and daily papers were probably premature can scarcely be denied; but that the work itself of these two investigators must be highly complimented and must eventually prove greatly creditable to American science we are proud to acknowledge. Moreover, we intend to show our pride in these investigations in a practical way, namely, by giving them the principal place in this article and devoting the space which we consider necessary to make them intelligible.

The Toxic and Antitoxic Effects of Ions. The paper during the past year which probably shows best the position of the subject at present is by Loeb[1] himself, on the toxic and antitoxic effects of ions as a function of their valency and possibly their electrical charge. How this subject first came to be taken up he himself relates as follows:

"Five years ago I published a series of papers on the physiological effects of the electric current, which impressed upon me the long-known fact that the galvanic current is the most universal and effective stim-

[1] American Journal of Physiology, 1902, vi., 6, p. 411.

ulus for life phenomena. This fact suggested to me the idea that it should be possible to influence life phenomena just as universally and effectively by the electrically charged molecules—the ions—as we can influence them by the electric current. From that time on the whole working force of my laboratory was devoted to the investigation of the physiological effects of ions."

His first aim was to find out whether or not it was possible to alter the physiological properties of tissues by artificially changing the proportion of ions contained in these tissues. In this way originated the investigations on the effect of ions upon the absorption of water by muscles, the effects of ions upon the rhythmical contractions of muscles and medusæ, the heart of the turtle, and the lymph hearts of the frogs, the rôle of ions in chemotrophic phenomena, and the influence of ions upon embryonic development, and the development of unfertilized eggs (artificial parthenogenesis).

The next step taken consisted in proving that it was indeed the electrical character of the ion that determined its specific efficiency. He succeeded in doing this three years ago. It was known that a frog's muscle gives rise to twitchings or rhythmical contractions when immersed in certain solutions. He showed that such contractions occurred only *in solutions of electrolytes, and not in solutions of non-conductors* (distilled water, various sugars, glycerin, and urea).

In the physiology of the heart the statement is frequently encountered that calcium is the stimulus for the contraction of the heart. He found, however, that a muscle is able to twitch rhythmically when immersed in the solution of salts with a monovalent kation—for instance, in Na, Li, Rb, and Cs salts—but that the addition of a small quantity of bivalent kation Ca, Mg, Sr, Ba, Be, Mn, Co inhibits these rhythmical contractions. This seemed to be a direct contradiction to the statement that calcium salts are the "cause" of the heart-beat. The significance of the calcium had to be looked for then in another direction. He soon found that the muscle, the apex of the heart, and a medusa contract rhythmically in a pure sodium chloride solution, but that they soon come to a standstill, while if a trace of soluble calcium salt is added to the sodium chloride solution, the contractions continue much longer. He concluded from this that the pure sodium chloride solution acts in the long run as a poison—that is to say, brings about definite but at present unknown physical changes in the protoplasm—but that a trace of calcium salt annihilates this toxic action.

Soon after he succeeded in demonstrating conclusively the poisonous effect of pure sodium chloride solution, and the annihilation of this effect by calcium. The eggs of the marine fish—fundulus—develop normally in sea-water, but they can develop just as well in distilled

water. The addition of ions from the outside is consequently not necessary to the development of this animal. He found now that if the freshly fertilized eggs of this fish are put into a pure sodium chloride solution having a concentration equal to the concentration of the sodium chloride in the sea-water (about $\frac{5}{8}$ m) not a single egg can develop into an embryo. If, however, a trace of a calcium salt is added to the sodium chloride solution, as many eggs develop and in just as normal a manner as in ordinary sea-water. The calcium ions in this case undoubtedly serve the purpose of annihilating the poisonous effects of a pure sodium chloride solution. In the meantime he had become familiar with the brilliant experiments of Hardy upon the influence of ions and the galvanic current upon colloidal solutions. They indicated that the next step was to see whether or not the valency and the sign of the electrical change of an ion determine its physiological effects. He suspected that the antitoxic effect of the calcium ion in the above-mentioned experiment was due to its electrical charge, and decided to investigate in a more systematic way whether or not the sign and quantity of the electrical charge influence life phenomena. His experiments carried on at Wood's Holl last summer showed conclusively that this is the case for the production of rhythmical contractions through ions. It seems at least possible that it is true also for artificial parthenogenesis.

First of all, the toxic effects of pure sodium chloride solutions at various concentrations were tested. It was found that high concentration of NaCl inhibited development, while traces of Ca negatived this effect. It was next shown that Sr, Ba, and Mg ions are also capable of annihilating the poisonous effects of a pure NaCl solution in a way similar to that of Ca ions. The same was proven also for Ba, Mg, Sr, Zn, and Fe. He even tried the antitoxic effect of ions as poisonous as copper and mercury, but with negative results, though with lead he had distinct success.

Experiments were now made to see if it were possible to annihilate the toxic effects of a sodium chloride solution through the addition of salts having a trivalent ion; $AlCl_3$, $Cr_2(So_4)_3$, and $FeCl_3$ were used. The experiments with $FeCl_3$ all yielded negative results, experiments with the other two were positive. It is worthy of note that the amount of a trivalent kation capable of exerting a certain antitoxic effect is considerably less than the amount of a bivalent kation necessary for the same purpose. Since traces of trivalent kations and small amounts of bivalent kations suffice to thus annihilate the poisonous effects of a sodium chloride solution, experiments were made to ascertain if the same could also be brought about by monovalent kations; the experiments have thus far led to no positive results.

Not only can the poisonous effect of a pure sodium chloride solution be annihilated by the addition of small amounts of bivalent or trivalent kations, but it seems as if the same holds for all salts which, like NaCl, have a univalent kation and anion. For instance, no embryos develop in a $\frac{2}{3}$ m Li, Cl solution, though the addition of small amounts of $Ca(NO_3)_2$, $BaCl_2$, $SrCl_2$, or $MgCl_2$ changes the results.

Consequently he feels justified in making the statement that the salts of monovalent kations (Na, Li, K, NH) with monovalent anions (Cl, NO_3, CH_3, COO) exert a toxic effect at certain concentrations. This toxic effect can be annihilated through the addition of a small amount of salt having a bivalent kation. For NaCl, proof has been brought forward that trivalent kations exhibit even a much more energetic antitoxic effect than bivalent kations.

Further experiments were instituted in which an attempt was made to annihilate the poisonous effects of NaCl by the addition of salts having a univalent or bivalent or trivalent anion, but the results were negative throughout; in other words, the toxic effect of salts with a monovalent kation and a monovalent anion can be annihilated only by bivalent or trivalent kations and not by monobitrivalent or trivalent anions.

If, in these experiments, only the kations have an antitoxic effect, and this the greater, the greater their electrical charge; and if in these antitoxic effects we are dealing only with electrical effects, then it is to be logically expected that the *toxic* effects which are inhibited in these cases are also electrical effects.

He goes on then into theoretical considerations, which tend to prove that the thermodynamical theory of life has utterly failed to show how thermal energy produced through the splitting up and oxidation of foodstuffs can lend to muscular contraction. He throws out Engelmann's explanation, and takes a view in harmony with that of Hardy and D'Arsonval, dependent on the theories in vogue in regard to the phenomena of coagulation in colloidal material. This view has already been exploited in the popular magazines and daily papers, so that it is scarcely necessary to discuss it here. He believes that the fact that ions may act toxically through their electrical charges, and that ions with the opposite charges may act antitoxically, may open a new and very fertile field for pathology and therapeutics.

On the Power of Na_2SO_4 to Neutralize the Ill-effects of NaCl. Despite Loeb's assertion, however, that the toxic effect of salts with a monovalent anion can be annihilated only by bitrivalent or trivalent kations and not by monobitrivalent or trivalent anions, Moore[1] showed, from a series of experiments on tadpoles and mosquito larvæ, that this

[1] American Journal of Physiology, 1902, vii., 3, p. 315.

is not absolutely true. Her results show that, in one case at least, it is possible to annihilate the poisonous effects of a salt with a monovalent kation and a monovalent anion by a bivalent anion—namely, the toxic effect of NaCl by Na_2SO_4. Still, from further experiments, it seems evident that this is not the immediate result of the bivalency of the anion, but some other effect not yet intelligible.

Concerning the Poisonous Effects of Pure Sodium Chloride Solutions upon the Nerve Muscle Preparation. Cushing[1] reports some work on the poisonous effect of pure sodium chloride solution upon the nerve muscle preparation that is more or less in line with Loeb's work, and may be mentioned here. His results are practically confirmatory of Locke's, though more precise, since they were obtained by infusion methods in a comparatively intact animal, rather than by simply immersing an isolated nerve and muscle in a bath. His conclusions are that pure sodium chloride solutions are injurious to the nerve-muscle preparation, the effect being, in a measure, related to the percentage of this salt in solution.

This injurious effect may be promptly counteracted by the blood or serum of certain animals, or by the proper "physiologically balanced salt solutions," which contain such ions, and in such proportions as to completely annihilate the poisonous effects which each constituent would have if it were alone in solution (for instance the so-called Ringer's solution).

An Analysis of the Influence of the Sodium, Potassium, and Calcium Salts of the Blood on the Automatic Contractions of Heart Muscle. Howell[2] disputes Loeb's expression that sodium chloride solutions will not support automatic contractility because they are *poisonous*, and affirms that the emphasizing of this is at least unfortunate. As a matter of fact, every other substance soluble in water, when taken alone, is also, so far as is known, poisonous to the heart muscle in the same sense. Pure solutions of salts of calcium, potassium, or other elements, as well as solutions of non-electrolytes, such as sugar and urea, are totally unable to support rhythmic activity of the heart muscle. To say that pure solutions of sodium chloride are poisonous to the heart muscle is to say nothing more than that solutions of sodium chloride alone will not maintain irritability and automatic contractility of the heart tissue; but the same is true to a more marked extent of every known constituent of the blood when taken alone.

Howell continues: "The really remarkable thing about NaCl is that in pure solution of appropriate concentration it is less injurious to living matter than any other substance. The universal employment

[1] American Journal of Physiology, 1901, vi., 2, p. 77.
[2] Ibid., 1901, vi., 4, p. 181.

of physiological saline in histological and physiological work upon living tissue bears witness to the fact."

Loeb's interesting discovery that the young fundulus will live indefinitely in distilled water, but dies in a short time when placed in a $\frac{5}{8}$ m solution of NaCl does not alter this fact at all, so far as Howell can see. The fundulus dies in pure solutions of NaCl, but under such conditions we may suppose that its diffusible Ca, K, etc., are lost, as would be the case if the heart or any of its tissues were bathed in the solution directly.

Howell's elaborate series of investigations were directed toward the analysis of the influence of the sodium, potassium, and calcium salts of the blood in the automatic contractions of heart muscle. He states the previous position as follows:

Loeb has imagined the existence of compounds of the metallic ions with the proteids, but although there is every reason to believe that the proteids may form dissociable compounds with either the kation or the anion, or possibly with both, the existence of such compounds has not been demonstrated experimentally; and even granting their existence, no clearer idea is obtained of the connection between the inorganic salts and the periodic katabolisms of rhythmically contracting muscle.

Confining ourselves to experimental facts, it would seem that we are not justified in going beyond the statement of Merunowicz—namely, for the heart contractions both organic and mineral constituents are necessary, the former supplying compounds from which energy is obtained; the latter giving to these compounds such a form that they can be used in the production of contractions.

From his own work he summarizes: Spontaneous contractions of the ventricular muscle of the terrapin's heart are dependent upon the presence in the tissue of dissociable compounds of both calcium and sodium. If either the Ca or the Na is absent, automatic contractions are impossible. Sodium salts (NaCl) in the liquid surrounding the heart tissue tend to produce a relaxation from loss of tone. Calcium chloride, on the contrary, causes shortening from increase of tone, which may pass into a permanent rigor. Potassium chloride exhibits an antagonistic effect toward the action of calcium chloride, but only to a marked extent when sodium salts are also present in approximately normal proportions.

The influence of the potassium ion when present in physiological proportions is shown by a slowing of the rhythm or a lengthening of the refractory phase. Under the combined influence of Ca, Na, and K the automatic contractility is maintained for longer periods than by the action of Na and Ca alone.

The fact that ventricular strips do not contract spontaneously, as a rule, in the animal's own serum, or in an equivalent Ringer's mixture, is due to the inhibitory influence of the potassium salts. The characteristic series of beats obtained by immersing a fresh strip of ventricle in a 0.7 per cent. solution of NaCl is referable to the following changes: 1. The latent period and the beginning of the series of spontaneous beats is due to the gradual loss of dissociable potassium from the strip of diffusion. 2. The gradual diminution and final disappearance of the beats is due to the loss of the dissociable calcium by diffusion.

On the Effects of Solutions of Various Electrolytes and Non-conductors upon Rigor Mortis and Heat Rigor. Moore,[1] with her usual thoroughness, studied the effects of solutions of various electrolytes and non-conductors upon rigor mortis and heat rigor.

The work was done for the purpose of ascertaining the effects of certain solutions upon the temperature for the sudden coagulation of proteids in the muscle *in situ*, and, second, the time necessary for coagulation at room temperature.

Halliburton (1884 to 1888) thought that he obtained four proteids from muscle plasma: paramyosinogen coagulating at 47° C., myosinogen at 56° C., and myoglobulin at 63° C., muscle albumin at 73° C., and myoalbumose, not coagulable by heat. Von Furth (1896 to 1900) and Stewart (1899) think that only two proteids have been isolated with certainty from muscle plasma, paramyosinogen, a typical globulin coagulable at 45° C. to 50° C., and myosinogen, an atypical globulin coagulable at 50° C. to 65° C. In this regard Moore agrees with von Furth and Stewart.

General conclusions are that hypotonic solutions and other solutions in which much water is absorbed, lower the temperature of coagulation and shorten the time of completion of rigor. Acids increase the temperature of opalescence and lower the temperature of coagulation, the amount of lowering increasing with the degree of dissociation. Alkalies lower the temperature of opalescence and increase the temperature of coagulation. In alkalies a specific influence is present which may find its explanation in the formation of some such alkali compound as Starke suggests. Rigor occurs readily in acids and alkalies at room temperature, but it is incomplete, for the coagulum tends to dissolve in these substances and also to some extent in some salt solutions. The dissolution is not a case of reversibility, for when once completely coagulated the proteids of muscles do not resume their original character. The chlorides in solutions isosmotic with $\frac{n}{8}$ NaCl show practical uniformity; the temperature of opalescence is raised, that of coagulation is only

[1] American Journal of Physiology, 1902, vii., 1, p. 1.

slightly affected. In other concentrations, variation occurs in wide limits; with the exception of $CaCl_2$ the temperature of opalescence in them is lowered, while the temperature of coagulation is lowered in weak solutions, raised in strong solutions.

Rigor occurs readily at room temperature in strong solutions of NaCl, Na_2SO_4, and $MgSO_4$, in $CaSO_4$, in all strengths of $CaCl_2$ and $(NH_4)SO_4$, and in other Ca precipitating solutions. It also occurs in KCl, but this substance is not a good coagulant. The effect of $MgCl_2$ is relaxing; rigor occurs only in $\frac{n}{2}$ concentration.

Ca precipitating solutions affect the coagulation temperature somewhat differently from Ca solutions. Ca, however, is not essential for the coagulation of muscle proteids, unless the small amount retained in the tissues is sufficient, for coagulation takes place in Ca precipitating solutions and also in non-conductors. Although the entrance of water favors coagulation and lowers the coagulation temperature, coagulation phenomena cannot be explained entirely on the basis of osmosis, for, after a certain concentration is reached, further increase in concentration may cause either increase or decrease in temperature. The nature of the ions present is a determining factor.

Normal rigor is not comparable to ordinary muscular contraction, for (1) heat rigor may be added algebraically to contraction; (2) rigor is not reversible. Heat rigor is not essentially different from normal rigor. Normal rigor is probably due to the lowering of the coagulation temperature of muscle proteids caused by the unwonted presence or juxtaposition in the tissue of acid, H_2O, or of certain salts.

The Prolongation of the Life of the Unfertilized Eggs of Sea-urchins by Potassium Cyanide. Another paper of Loeb's (Loeb and Lewis[1]), published during the year, was taken up by the sensational journals as relating to the elixir of life. Its actual title was that given at the beginning of this paragraph.

In a former paper Loeb pointed out that the experiments on artificial parthenogenesis have a bearing upon the problem of the prolongation of life. The unfertilized mature eggs of a sea-urchin die comparatively soon when deposited in sea-water. The same eggs, however, live a longer time when caused to develop either artificially, by extracting a certain quantity of water from them, or naturally, by allowing a spermatozoon to enter. Loeb concluded from this that there are two kinds of processes going on in the eggs; one which leads to the death and disintegration of the egg—a mortal process; and a second which leads to cell divisions and further development. The latter process inhibits or modifies the mortal process.

[1] American Journal of Physiology, 1902, vi., 5, p. 305.

With this assumption the problem of the prolongation of the life of a cell was given a concrete form. According to this idea death and disintegration are due to specific processes which take place in the egg, and possibly in other or all living matter. These processes must be checked in order to render life possible. If this theory were of any value it were certain to lead to the discovery of artificial means by which the life of unfertilized eggs might be prolonged.

The specific life phenomena are, as far as their chemical side is concerned, chiefly, if not altogether, catalytic phenomena. Hence, it was to be expected that a checking of the specific mortal processes should be brought about by agencies which inhibit catalytic phenomena without permanently altering the constitution of living matter.

Among all the agencies which act in this way, potassium cyanide seemed to meet this condition most perfectly. It weakens or inhibits a number of enzymatic processes in living matter without necessarily altering the condition of the latter. When the potassium cyanide is permitted to evaporate, the original condition of the system may be restored.

A series of experiments on the effects of KCN on the unfertilized eggs of sea-urchins confirmed these expectations and proved that by adding a small quantity of KCN to sea-water the unfertilized eggs of the sea-urchin can be kept alive a comparatively long time, at a temperature of 20° C. or above.

The investigators continue in these words: "As long as we consider death as something merely negative (namely, the cessation of certain processes), it must appear extremely paradoxical that the life of the unfertilized egg of the sea-urchin should be prolonged by applying one of the most deadly poisons. But the paradoxical element disappears when we start from the assumption which led us to these experiments—namely, that in the unfertilized eggs specific mortal processes are going on which are checked or modified by the process of sexual or osmotic fertilization. These specific mortal processes are also checked by potassium cyanide, which substitutes for the destructive action of these processes a condition of suspension of life ('vie latente' of Bernard)."

In regard to the next question, What is the nature of the mortal processes in the unfertilized egg, and how can fertilization check them? no definite answer is possible at present. The mortal processes may consist in self-digestion, or in other enzymotic processes, or they may not be catalytic at all. How the act of fertilization can modify or check such processes is not beyond analogy. We know that a full supply of oxygen decreases the fermentative action of zymase. Spitzer has made it probable that the cell nucleus contains an oxidizing agent,

namely, the nucleoproteids. The process of fertilization results in the egg of the sea-urchin, in a rapid series of successive cell divisions, in each of which the contents of the nucleus are scattered throughout the cell. It is easily conceivable that this periodic spreading or mixing of the contents of the nucleus and the cells may modify the chemical processes in the egg and check the mortal processes.

At Loeb's[1] suggestion, Lyon endeavored to ascertain whether the degree of resistance to KCN poison remained constant or varied during the progress of development of the eggs. He found that there was a loss of resistance, and that "probably each cleavage from the very first increases the susceptibility."

Artificial Parthenogenesis. Since Morgan's and Loeb's original work in artificial parthenogenesis, results have been obtained in a number of simple ways that would sound ridiculous to the early investigators. Many of these experiments are reported this year. We may quote a few of them.

Matthews[2] shows that mechanical agitation of eggs of the star-fish (asterias forbesii) without any change whatever either in the chemical constitution or the osmotic pressure of the sea-water is capable of giving rise to artificial parthenogenesis. The mechanical disturbance necessary to start the process is in certain conditions of the eggs so slight as to render this a serious source of error in experiments.

Fischer[3] has shown that the same is true for amphitrite and chætopterus. He further believes that his experiments upon amphitrite and nereis confirm the views of Loeb that the spermatozoon does not act as a "stimulus" to the egg that starts its development, but simply as a catalyzer that accelerates a process which starts of its own accord. The unfertilized eggs of either amphitrite or nereis, if left undisturbed in sea-water, show a dissolution of the nucleus, a deepening in the color, and a contraction of the protoplasm, together with a beginning cellular division that correspond to the changes which occur in the fertilized egg, except that they begin at a much later time, and succeed each other much more slowly than in the fertilized eggs. The addition of calcium (in amphitrite), or the abstraction of water (in nereis) from the egg serves only as a method of accelerating a process that occurs anyway. But this accelerated karyokinesis is essential to the further development of the egg, for if left undisturbed in sea-water the egg reaches only the first stages of the segmentation and then dies.

Greeley[4] succeeded in bringing the unfertilized eggs of the star-fish (asterias forbesii) to the bipinnaria stage by simple lowering of the

[1] American Journal of Physiology, 1902, vii., 1, p. 56.
[2] Ibid., 1901, vi., 2, p. 142.
[3] Ibid., 1902, vii., 3, p. 301.
[4] Ibid., 1902, vi., 5, p. 296.

temperature. The temperature required is about 7° to 4° C. He failed to produce the same by raising the temperature of the sea-water, contrary to the results obtained by Delage, who apparently took no precautions against agitation, which may account for the difference.

Hunter,[1] in experiments with sea-water concentrated by evaporation, confirmed Loeb's osmotic theory of artificial parthenogenesis in arbacia. Sea-water that is condensed until it is isotonic with Loeb's 10 to 15 per cent. $2\frac{1}{2}$ m sodium chloride solutions will cause artificial parthenogenesis. Sea-water with osmotic pressure perceptibly less or greater than the 10 to 15 per cent. solution of $2\frac{1}{2}$ m sodium chloride will not produce artificial parthenogenesis.

In experiments with the common blue-green Stentor coeruleus, Arthur Greeley[2] showed it probable that a reduction of the temperature and a loss of water have similar effects, because the cell loses water when the temperature is lowered as well as when the concentration of the surrounding medium is raised.

The determination of the essential fecundative qualities in fertilization has always been an interesting subject to physiologists, yet so far the experiments have not met with decided success. Various common enzymes have been tentatively tried in order to see if they could bring about development, but the results never justified any positive conclusions. Instead, therefore, of working from the negative side Gies[3] sought an enzyme in the extract of spermatozoa. His results were negative, yet they by no means deny such an enzyme, and this still remains a fertile field of investigation.

The Action of Pilocarpine and Atropine on the Embryos of the Star-fish and the Sea-urchin. With this end in view, Matthews,[4] sought the action of pilocarpine and atropine on animal cells directly by studying their influence on the development of the star-fish (asterias forbesii) and the sea-urchin (arabacia punctulata). He found that atropine sulphate in small doses hinders the development of arbacia and asterias larvæ and gives rise to dwarf embryos.

Pilocarpine hydrochlorate hastens development of the asterias larvæ and gives rise to abnormally large embryos.

Hence atropine and pilocarpine act on animal cells directly, and they are not confined in their action to secretory nerve ends.

The nature of their action suggests that atropine inhibits the oxidations taking place in the cells, while pilocarpine increases those oxidations.

Atropine may stop secretion by checking the oxidative decompositions

[1] American Journal of Physiology, 1901, vi., 3, p. 180.
[2] Ibid., vi. 2, p. 122.
[3] Ibid., p. 53.
[4] Ibid., vi., 4, p. 207.

in protoplasm so that there is no normal increase in osmotic pressure during vasodilation, and secretion does not occur. Pilocarpine, by hastening these decompositions, increases osmotic pressure, and thus secretion. Both drugs probably act directly on the gland cells. The evidence that they do not act on secretory cells, but on the ends of the secretory nerves, is insufficient.

The work of Heidenhain and Langley seemed to show that pilocarpine and atropine do not affect gland cells, but only the endings of the hypothetical secretory nerves. The chief evidence of this is the observation that atropine stops the secretion which normally occurs in the submaxillary gland of the dog upon stimulation of the chorda tympani, but not that which follows stimulation of the cervical sympathetic. This fact indicates either that the secreting cells are not poisoned by atropine, or that the sympathetic causes secretion in some other way than by acting on these cells. There is no evidence, except in the salivary glands, that atropine has not poisoned the secreting cells, for in no other glands have two secretory nerves been found, one of which is paralyzed by the drug, while the other is not affected.

A Contribution to the Chemistry of Proteids. In 1901 Hopkins and Cole[1] showed that the color reaction of proteids described by Adamiewicz is obtained only when glyoxylic acid is present in the acetic acid employed. Since there is no evidence that this color reaction depends upon carbohydrate groups in the proteid molecule it becomes of interest to know what molecular groups are responsible for it. With this in view, they endeavored to separate such a substance from the products of proteolysis, and finally succeeded in preparing a beautifully crystalline product, which gives the glyoxylic reaction in a typical manner.

The method is as follows: After digestion of the case in preparations until the tryptophane reaction obtainable from the product has reached a maximum, the mixture is heated to 80°, and, after cooling, filtered. To the clear filtrate strong sulphuric acid is added in such quantity as roughly to equal 5 to 6 per cent. of filtrate by volume.

The mercuric sulphide reagent (10 per cent. of the salt dissolved in 5 per cent. of sulphuric acid) is now added. The preparation is now allowed to stand for about twelve hours, when a bulky lemon-yellow precipitate settles out. This is filtered off and washed with 5 per cent. sulphuric acid. The first washings give a marked red color on the addition of Millon's reagent in the cold. The washing is continued until this has disappeared and Millon's reagent is found to give only a brownish-yellow coloration. The mercury compound of tyrosin is thus washed away. The washed mercury precipitate is suspended in about

[1] American Journal of Physiology, 1901, xxvii., 4 and 5, p. 418.

half a litre of water and decomposed with sulphuretted hydrogen, which is repeated. It is then filtered and the filtrate freed from the greater part of the hydrogen sulphate by boiling. It is then cooled and treated once more with 5 per cent. of its volume of sulphuric acid as a preliminary to reprecipitation by mercury. Cystin is then removed. The sulphuric acid which is liberated on decomposition of the mercury compound is next removed from the filtrate by means of barium hydrate. After some digestion on the water bath the bulky precipitate of barium sulphate is filtered off, the filtrate is now mixed with about its bulk of 90 per cent. alcohol and evaporated on the water bath. Evaporation is continued, with the occasional addition of small quantities of alcohol, until the solution on removal from the bath sets to a thick magma of crystals. These are filtered off at the pump, thoroughly drained, and washed with 90 per cent. of alcohol. They are redissolved in a minimum quantity of hot water, an equal bulk of 90 per cent. of alcohol is added, and the solution is boiled with a little animal charcoal and filtered hot. On concentration fine white pearly plates separate. The yield of crude product is apparently about 1 per cent., but a maximum yield is not yet known.

After the treatment described the product is obtained in the form of fine white glistening plates of highly characteristic appearance. The substance is moderately soluble in cold water and freely soluble in water at 100°. Its aqueous solutions are markedly acid to litmus. It is but sparingly soluble in absolute alcohol, cold or hot, but the solubility increases rapidly on dilution of the spirit, and it may be conveniently recrystallized from hot alcohol of 75 to 80 per cent.

It is moderately soluble in methyl alcohol, but well formed crystals are not easily obtained from the solvent; fine plates are gotten, however, if a methyl alcohol solution be mixed with chloroform and evaporated in vacuo.

The substance does not show a well-defined melting point, but its behavior on heating is sufficiently characteristic. It begins to change color at 220° and is brown at 240°; it then softens, and at 252° is fully melted, the final stage of fusion being fairly sharp. A little above its melting point there is a brisk evolution of carbon dioxide, and at a higher temperature an abundant yield of indol and skatol.

Solutions of the substance yield the glyoxylic color-reaction with great intensity. In moderately strong solutions, if sufficiently glyoxylic acid be present, the addition of sulphuric acid produces a deep indigo color, a greenish zone being seen next the acid when the latter is allowed to remain subnatant. With weak solutions the color is exactly that given by the original proteid, and the spectroscopic absorption is precisely similar. A solution containing 1 part in 10,000 gives a well-marked color. The substance gives also the tryptophane reaction.

METABOLISM.

Phlorizin Diabetes. Lewandowsky[1] concludes, from the results of a series of experiments on rabbits, cats, and dogs, that the theory of V. Mering, according to which the diabetes which follows the administration of phlorizin is due a primary excretion of the sugar by the kidneys, has more probability than the theories of Levene, Coolen, Biedl, and Kolisch. He assumes that the phlorizin damages the secreting renal epithelia to such an extent that they lose their normal impenetrability to the sugar ordinarily circulating in the blood.

Chromic Acid Diabetes. To the many substances which produce a more or less prolonged glycosuria—*e. g.*, cocaine, veratrine, morphine, caffeine, phlorizin, etc., Kossa[2] now adds chromic acid. From a series of experiments he concludes as follows: Of the chromic acid compounds the greater number, and especially the potassium chromate, produce in different warm-blooded animals a glycosuria, which, however, is most pronounced in the dog. The effect is greater when injected subcutaneously in dilute solution than when given by the mouth. The glycosuria of the rabbit is very moderate, but fluctuates within wide limits. The chromic acid diabetes belongs to the group of the so-called renal diabetes, because during its use, as in the case of phlorizin, the amount of sugar in the blood does not increase, even if the excretion of the urine is interfered with.

As to the Position of the Purin Bodies in Human Metabolism. Burian and Schur,[3] continuing their experiments on human beings and mammals, report that in all mammals, the exogenous as well as the endogenous, uric acid is an intermediate substance that is a product of metabolism, which undergoes a still farther destruction in the body. The correctness of their view, even for the endogenous uric acid, follows from the fact that (in dogs) after exclusion of the kidneys and of the most important organ for the destruction of the uric acid, the liver, endogenous uric acid is found in the blood, while this is not the case after the exclusion of only the kidneys. But, although the mammalian body has the power of destroying the exogenous and endogenous uric acid, and although the uric acid destroying power of the single organ possessing this power is far-reaching, still, a fraction of the circulating uric acid is always excreted unchanged, because the kidneys take it out of the blood before it is changed. If more blood flows through the kidney the amount of the excreted fraction of uric acid increases.

[1] Archiv f. Physiologie, 1901, S. 365.
[2] Archiv f. d. ges. Physiologie, Band lxxxviii., S. 627.
[3] Ibid., Band lxxxvii., S. 229.

Such changes, however, are compensated for again later on, so that the average in twenty-four hours of the excreted uric acid is a pretty constant amount, in consequence of which there may be determined for each individual a certain factor—the integrative factor—with which the excreted uric acid must be multiplied in order to obtain the amount that has entered the circulation.

The integrative factor is constant, even for different human beings, though it varies in different carnivorous animals. Man excretes about one-half of the circulating uric acid, because in him probably as much blood flows through the kidneys as through the organs of uric acid destruction. One-half is excreted, the other half is destroyed in the body.

The Influence of Alcohol upon Albumin Metabolism. From a comprehensive and critical review of this question and from new experiments conducted by him on man, Rosemann[1] concludes that most (more than 90 per cent.) of the ingested alcohol is oxidized in the human system and that the potential energy furnished by it is just as much an albumin-saving agent as an equivalent amount of carbohydrate or fat. But, at the same time, there is exerted upon the albumin a harmful effect by the alcohol, due to its deleterious influence upon the cells of the body, and which more or less counteracts its albumin-saving effects. The harmful action of alcohol upon the tissue cells, which is obscured during the first few days of its ingestion, later decreases, and finally ceases altogether, because the cells, to a certain degree, become accustomed to it. After this period its effect is mainly fat and albumin saving; the remote injurious effects which alcohol has upon all the organs of the body, if taken in large amounts and for a long period of time, exclude it from the class of foods in a healthy person. The author would not recommend it either as a food for patients with febrile infectious diseases as long as sufficient nourishment can be given in other forms, and especially that of sugar. The author distinctly stated, however, that his remarks refer only to the employment of alcohol as a food in disease. The use of it as an antipyretic, excitant, and appetizing remedy must be judged by totally different considerations.

Phosphate Metabolism. We have as yet no alteration of metabolism that can be said to correspond to mental derangement, consequently the following study of Folin and Shaffer[2] is very interesting. They had the good fortune to procure a case in the McLean Hospital for the Insane, in which the patient's condition alternated with absolute regularity from day to day, being one day little removed from the normal, while quite disturbed on the other.

[1] Archiv f. d. ges. Physiologie, Band lxxxvi., S. 307.

[2] American Journal of Physiology, 1902, vii., 1, p. 135.

This condition, which had lasted uninterruptedly for several months, presented an unusual opportunity for trying to discover some alteration in the metabolism of the patient corresponding to the alteration in the mental symptoms. Any sufficiently characteristic alteration in the patient's metabolism was deemed important, because so far no normal metabolism whatever can be said to be characteristically associated with any of the mental diseases.

The existence of an unmistakable periodicity in the elimination of phosphoric acid through the kidneys, which was high on the nervous days and low on the alternate good days, they consider proved by the analysis and experiments.

The Excretion of Nitrogen during Nervous Excitement. As a note of encouragement to further studies in the same regard, we may mention two experiments of Benedict[1] on the excretion of nitrogen during nervous excitement.

The ideal conditions for such an experiment demand a preliminary period of several days in which the subject is given a diet with constant nitrogen supply. All nervous excitement should be carefully avoided. When the system is about in nitrogen equilibrium the subject should be placed under strong nervous excitement, the diet remaining the same. To secure this last condition, the writer attended on two successive years one of the great intercollegiate football games. The results of these two experiments would seem to indicate that nitrogen metabolism undergoes no noticeable change during periods of intense nervous excitement. It is by no means certain, however, that long-continued anger, sorrow, or fear would not produce disturbances of nitrogen metabolism other than those that could properly be ascribed to a derangement of digestive functions. It is further to be said that the effect of nervous excitement accompanying personal effort, such as, for example, the feeling of sudden and great responsibility, should be thoroughly investigated before drawing any final conclusions regarding nitrogen metabolism during nervous excitement.

A Study of the Metabolism in Dogs with Shortened Small Intestines. The effect of excision of various parts of the gastro-intestinal canal upon metabolism and upon the nutritive value of the foodstuffs has been a subject of considerable study to numerous observers. Such studies possess a double interest. On the one hand, the physiologist looks to this method of excision for the light that it may throw on the normal function of the various parts of the intestinal tracts, and, on the other hand, the operation is of considerable practical interest to the physician and the surgeon.

[1] American Journal of Physiology, 1902, vi., 6, p. 399.

With this in view, Erlanger and Hewlett[1] made a study of the metabolism in dogs with shortened small intestines. Their conclusions are as follows: Dogs from which 70 to 83 per cent. of the combined jejunum and ileum have been removed may live indefinitely after recovery from the operation. Their nutrition may appear to be perfectly normal or it may be so poor that even when eating ravenously they do not seem to be able to keep well nourished.

Such dogs are peculiarly liable to be affected with diarrhœa, which may be caused by a diet too rich in fat or one containing too much inert non-digestible material. This diarrhœa is of very serious moment to such a dog, and may cause its death.

The urine of such dogs shows no great variation in quantity, specific gravity, or nitrogenous contents from that of normal animals.

The conjugated sulphates in the urine are increased absolutely and relatively to the alkaline sulphates, indicating an excess of intestinal putrefaction.

The quantity of feces varied in the two animals. In the dog from which 70 per cent. of the movable small intestine had been removed there was no marked increase of feces; in the dog from which 82 per cent. had been removed the amount of feces was increased.

The percentage of water in the feces of dogs deprived of large amounts of small intestine may equal or only slightly exceed the percentage of water in the feces of normal dogs. This in contrast with the increased percentage of water in the feces of animals deprived of the large intestine.

On a diet poor in fat the dog with a shortened small intestine absorbs the fat as well or almost as well as a normal dog. As the fat in the diet is increased the fall in the percentage eliminated in the feces which occurs in the normal animal may either occur to a lesser extent or may not occur at all in dogs deprived of the small intestine. With large amounts of fat in the diet 25 per cent. of that ingested may appear in the feces, whereas in our normal dog only about 4.5 per cent. appeared.

The addition of fat to the diet of a normal dog does not greatly affect the amount of nitrogenous material eliminated by the feces. The addition of fat to the diet of dogs deprived of small intestine causes an increased elimination of nitrogenous material in the feces. On a diet rich in fat the amount of nitrogen eliminated in the feces may be double that eliminated by a normal dog, although on a diet poor in fat there is no great difference between the two.

[1] American Journal of Physiology, 1901, vi. p. 1.

FOODS, DIGESTION, AND ABSORPTION.

The Liberation of Volatile Sulphide from Milk on Heating. The fact of the frequent occurrence of scurvy in children on a diet of milk sterilized by boiling has always made it an interesting question as to just what changes occur in boiled milk. The change in color, in odor, etc., of milk on boiling, the formation of a film on the surface, its less easy digestibility, all indicate a change in chemical composition. In order to make our knowledge more definite, Rettger[1] has studied this problem and gives us at least a suggestion. He found that on heating normal milk above 85° C., a partial decomposition of the milk proteid occurs, which is indicated by the liberation of volatile sulphide, in all probability hydrogen sulphide.

The amount of sulphur thus given off is very small, but it is sufficient in quantity to be easily recognized by the blackening of lead acetate paper and lead acetate cotton, and the discolorization of dilute potassium permanganate solution. Alkalies and alkaline-reacting phosphates facilitate this decomposition, while acids and acid-reacting phosphates retard it. Hence the amount of sulphide liberated depends largely on the reaction of the milk.

What part this liberation of sulphide may take in rendering milk injurious is a question of practical signification, but one which he does not pretend to answer, though he suggests that the alterations in the proteids permitting the liberation of volatile sulphide may have something to do with its injuriousness in case of prolonged use.

Although Rettger believes that the formation of the film on milk involves a chemical process, Jamison and Hertz[2] show that a similar film is produced on warming any proteid solution containing emulsified fat or paraffin. They consider that the film is probably formed of unchanged dried proteid in the case of non-coagulable proteids, and in that of coagulable proteids if the temperature is kept below their coagulation point. If the temperature is higher with the latter the film is composed, at any rate, partly of coagulated proteid.

On the Digestion of Cane Sugar. To clear up the contradictions which exist in regard to the digestion of cane sugar, Widdicombe[3] reports a series of experiments in relation thereto. It had been definitely affirmed (Brown and Heron), and as definitely contradicted (Shore and Tebb), that the parts of the intestine containing Peyer's patches were most active in hydrolizing maltose and inverting cane

[1] American Journal of Physiology, 1902, vi., 6, p. 450.
[2] Journal of Physiology, 1901, xxvii., 1 and 2, p. 36.
[3] Ibid., 1902, xxviii., 1 and 2, p. 175.

sugar than parts without these collections of lymphoid tissue. Widdicombe's experiments would go to prove that portions free from Peyer's patches are more active than those containing the patches. He also found that the intestinal mucous membrane of the pig inverts cane sugar freely.

The inverting action is not exercised in an acid medium, but the enzyme is not destroyed by acid, its action being merely suspended.

Lymphatic glands do not contain an inverting enzyme. The gastric mucous membrane contains an enzyme which acts in an acid medium, not in an alkaline one.

Proteids interfere with or stop the inverting action of dilute hydrochloric acid.

Gastric juice contains an inverting enzyme.

Saliva has no action on cane sugar.

The Conditions of the Formation and Secretion of Chymosin. Among the conclusions deduced from experimental work on the formation of the milk-curdling ferment of the stomach, by Winogradow,[1] may be mentioned the following: The formation of this ferment in the gastric mucous membrane increases from the first to the ninth hour after the taking of food. This occurs in two maxima, one in the second to the fifth, the other in the ninth to the eleventh hour.

The formation of pepsin shows the same picture as that of chymosin, as the curve of the amount of pepsin also shows two maxima, one in the fourth to the fifth, the other in the ninth to the eleventh hour. After the eleventh hour both chymosin and pepsin begin to decline very rapidly in amounts.

Between the physiological state of the secretory state of the stomach and the chemical elaboration of the stomach contents there exists a complete parallelism. The greatest amount of digested products accumulates in those hours in which the amount of the ferments in the mucous membrane and in the gastric juice is the greatest.

A Contribution to the Knowledge of the Movement of the Stomach. Glaessner[2] has recorded the results of a series of experiments performed on frogs with a view of disclosing the nerve mechanism involved. He employed as a stimulus various solutions, which were applied to both the inner (mucous) and the outer (serous) coats. It was found that when applied to the mucous coat hydrochloric acid, 0.3 per cent., lactic acid, 0.3 per cent., and salt solutions concentrated; grape sugar solutions concentrated; nicotine, $\frac{1}{6}$ per cent., and atropine, $\frac{1}{6}$ per cent., had no effect on the gastric movements, while alcohol, 15 per

[1] Archiv f. d. ges. Physiologie, Band lxxxvii., S. 170.
[2] Ibid., Band lxxxvi., S. 291.

cent., promptly produced a decided, almost tetanic contraction. Morphine, $\frac{1}{4}$ per cent., and chloral hydrate, $\frac{1}{6}$ per cent., almost completely arrested the gastric movements. The same substances when applied to the serous coat, however, produced quite different results. Thus, saline solutions and acids gave rise to decided contractions, while chloral and morphine were without influence in this respect. Nicotine excited contraction, as did alcohol. With reference to the gastric reflexes, it was found that these were excited not only from the higher parts of the digestive tracts (pharynx), but also from the lower parts (the intestine). The reflex movements of the stomach from the intestinal tract, however, were only called forth when the stimulus was applied to the serous coat and not the mucous coat. Glaessner believes from his experiments that the centre for the gastric reflexes does not lie in the medulla oblongata but in the spinal cord, and that the afferent path is through the mesenteric nerves and the efferent is through the spinal nerves.

The Conditions of Conversion of Pancreatic Zymogens into Enzymes. In exceedingly elaborate papers, which constitute most creditable contributions to physiology, Vernon[1] presents studies on pancreatic zymogens and enzymes. His manner of dealing with the subject is rather technical, yet we are using pancreatic extract to such an extent in therapeutics, as well as in physiological experiments, that everything on the subject is interesting.

The first paper relates principally to the manner of obtaining the most powerful extracts. In brief, he says: Extracts of a fresh pancreatic gland show no ferment activity for some days, and then more or less suddenly develop nearly their maximum power. For instance, a 25 per cent. alcoholic extract of an ox's pancreas was found to have a rennetic value of 1.7 after 5 days' extraction, and of 16.7 after 9 days; the normal saline extract of the same pancreas had a value of 78 after 13 days, and of 200 after 19 days; the aqueous and saturated salt extracts had values of respectively 16.8 and 3.9 after 19 days, and 200 and 295 after 33 days. After maintaining their maximum power for a few days or weeks the extracts gradually deteriorate.

When the glands from several different animals are minced together and extracted the ferment activity begins to develop at once. In the case of sheep glands the 25 per cent. alcoholic extract was found to attain its maximum tryptic (T) and rennetic (R) values in 12 days; in the normal saline extract its maximum T in 2 days, and its maximum R in 8 days; in the 75 per cent. glycerin extract its maximum T in 63 days, and its R in 86 days. In the case of pig's glands the alcoholic

[1] Journal of Physiology, 1901, xxvii., 4 and 5, p. 269, and Ibid., 1902, xxviii., 1 and 2, p. 137.

extract reached its maximum T in 9 days, and its R in 59 days; the normal saline extract its T in 5 days, and its R in 16 days; the glycerin extract its T in 71 days, and its R in 105 days. The glycerin extracts attained more than twice the T of the alcoholic extracts, and three to ten times that of the saline extracts, but the maximum rennetic values were comparatively little influenced by the nature of the extracting liquid. Still, as a rule, the tryptic and the rennetic powers of extracts show a distinct resemblance, but this is only qualitative, not quantitative. The relation between the R and T values may vary considerably from day to day in the same extract, and still more so in different extracts. Also the extracts of pig's glands, as compared with those of sheep's, contain relatively much more tryptic ferment.

The destructibility of the trypsin, as tested by keeping the diluted extract for one hour at 38° C. with 4 per cent. Na_2Co_3, and determining the percentage of ferment destroyed at the end of that time, varies concomitantly with the activity of the extract. Thus, the normal saline extract of sheep, when at its maximum proteolytic power (T 23.7), had 76.9 per cent. of its ferment so destroyed. When its T had sunk to 15.0, the destruction-rate fell to 51.7 per cent.; when to 9.5, to 38.2 per cent., and when to 5.7 to 19.6 per cent. The other extracts of sheep's and of pig's pancreas showed a similar increase of stability with decrease of tryptic power. The glycerin extract of sheep reached a (maximum) T of 72, and had no less than 80 per cent. of its ferment destroyed per hour. The glycerin extract of pig, with a T of 208, had only 69 per cent. destroyed, and the other extracts of pig were also slightly more stable than those of sheep, in spite of their having treble the tryptic power. Also the two glycerin extracts did not increase in stability, even after their T had fallen off respectively 47.9 and 139, hence, probably about one-half of the trypsin they originally contained was of the same degree of instability.

If filtered glycerin extracts of zymogen be diluted with water they spontaneously develop tryptic power at a rate increasing with the degree of dilution. If small quantities of an active extract be added in addition, the rate of conversion of zymogen into enzyme is enormously increased. For instance, the addition of 1 per cent. of active glycerin extract of pig's pancreas to inactive glycerin extract caused the T to increase from 0.85 to 88.1 in 2 days; the addition of 3 per cent., to 89.1 in 1 day; and of 10 per cent., to 97.5 in 9 hours. When no active extract was added the T increased only to 1.14 in 4 days. At 38°, instead of at room temperature, the rate of conversion is three or more times as rapid. On comparing extracts of pancreas of different animals it was found that their tryptic activity, and on their degree of instability (as regards Na_2Co_3), but proportionately to their tryptic activity, active

extracts set free the enzyme from the zymogen much more rapidly than the comparatively inactive extracts.

The rennet ferment in active extracts is set free as well as tryptic, but it was found that the liberation of the ferment from its zymogen was effected, not by the rennet ferment, but by the tryptic. Thus, if an extract containing a large amount of rennet ferment and but little tryptic were added to an inactive extract, there was but little liberation of either rennetic or tryptic ferment; but if one containing a small amount of rennet ferment and a large amount of tryptic were added, there was considerable liberation of both ferments.

In support of Langley's view of the existence of zymogens of various degrees of elaboration, it was found that an inactive extract, on keeping, showed a considerably increased susceptibility to the enzyme-liberating action of active extract; also a considerable part of the zymogen in gland tissue only becomes soluble after the gland has been left in contact with active extract.

It was found that the amount of ferment liberated by exposure of the minced gland substance to the air for twenty or more hours was, as a rule, very small, most of the ferment being set free after the addition of the extracting liquid. As a rule, also, exposure to the air destroyed more than half of the rennetic ferment, and more than three-fourths of the tryptic ferment.

Heidenhain's method of keeping gland substance for ten minutes with 1 per cent. acetic acid before mixing with glycerin did not prove successful in the case of pig's pancreas, but fairly active extracts were obtained by keeping the gland with 2 per cent. acetic acid for twenty hours before adding the glycerin, and also by adding the 0.05 to 0.25 per cent. acetic acid to the diluted glycerin extract and gland substance. The addition of acids to filtered extracts never in any case hastened enzyme formation, but always considerably retarded it. Ultimately, however, the zymogen underwent conversion into enzyme, even in the presence of 0.58 per cent. HCl, 0.19 per cent. acetic acid, and 0.21 per cent. lactic acid. The acid seemed to have no destructive effect on either enzyme or zymogen at room temperature, but this is not remarkable, as the natural acidity of kept extracts in which the ferments may remain undecomposed for months may be equivalent to 0.59 per cent. lactic acid.

The addition of small quantities of tryptic digestion products to inactive extracts was found to have a moderate enzyme liberating effect.

If oxygen or CO_2 were bubbled for one to three hours through diluted glycerin extract kept at 38° C., the enzyme was not liberated any more rapidly or slowly than unaërated extract. If, however, 1 per cent. of an active extract were added in addition, then in one hour the oxygen

increased the enzyme formation by respectively 43 per cent. and 28 per cent. in two different observations, while the CO_2 decreased it by respectively 6.4 per cent. and 12 per cent.

The second paper[1] deals with the making of pancreatic diastase. He says: On making aqueous, saline, alcoholic, and glycerin extracts of the minced pancreas of the pig, sheep, dog, ox, and of man, and on determining the diastatic power of such extracts from time to time, it was frequently found that during the first few days of extraction the ferment activity markedly increased. For instance, two dilute alcoholic extracts of sheep's pancreas increased in value from 6.2 and 5.9 on the first day of extraction to respectively 21 on the eighth day of extraction, and 25 on the twelfth day, and then gradually deteriorated. An alcoholic extract of ox pancreas increased from 3.4 on the first day to 12.1 on the fifth day. Glycerin extracts invariably showed an initial rise in value; the more dilute the glycerin, the more rapid being the rise. For instance, a concentrated glycerin extract of man's pancreas had a value of 6.3 after two days' extraction, and was still increasing in activity six months later, it then having attained a value of 41.7. A 50 per cent. glycerin extract of the same gland had a value of 21.6 after three days' extraction, and reached a maximum of 551 after twenty days. One must conclude that as long as such extracts show much increase in diastatic power on keeping, undecomposed zymogen is still present in the gland tissues. This zymogen is insoluble in any of the media employed, an extract filtered off from its gland substance never showing any rise in value. The initial rise in diastatic activity of extracts kept in contact with their gland substance is probably only in small part due to physical causes.

To prove this, some chipped fibrin was mixed with a very active glycerin extract for twenty-four hours, and most of the glycerin then expressed. On extracting this ferment-saturated fibrin with 75 per cent., 50 per cent., and 25 per cent. glycerin, and with 25 per cent. alcohol, it was found that three-fourths or more of the ferment passed into solution in twenty-four hours, while concentrated glycerin extracted 57 per cent. of the ferment in this time. Fresh liver tissue and old pancreatic tissue which had lost its diastatic activity yielded up the ferment with which they had been saturated more readily still.

The deterioration in the diastatic value of extracts is chiefly dependent on the temperature and on the natural acidity they develop. Thus, extracts made in August deteriorated much more rapidly than those made in April, and extracts kept at 38° C., instead of at room temperature, had about 94 per cent. of their ferment destroyed in two

[1] Supra cito.

days. The natural acidity, as determined by titration with 2 per cent-NaCO, is considerable, and may correspond to the presence of 5 per cent. lactic acid. As a rule, the extracts showed the most rapid deterioration when the acidity began to increase considerably (probably as the result of autodigestion). The addition of 0.35 per cent. HCl, 1.93 per cent. acetic acid, and 0.82 per cent. lactic acid to filtered extract destroyed almost all the ferment in twenty-four days, though there was a good deal left undecomposed after five or ten days.

On the Agents Concerned in the Production of the Tryptic Ferment from Its Zymogen. Bellamy[1] goes into the subject of the correlation of the spleen and the pancreas in the elaboration of the active tryptic ferment.

The pancreas of the dog presents two phases of activity: (*a*) A slow and continuous phase feebly evident after the decline of digestion, and reaching its culmen during complete fast; during this period zymogen is accumulating in the gland cells, and at this time the contents of the latter, although consisting for the most part of pure zymogen, may, if the previous intake of food be not copious enough to occasion its entire removal, include a certain amount of true trypsin. (*b*) A rapid and intermittent phase, coincident with the period of considerable gastric activity, in which, as advocated by Herzen, the inactive zymogen granules present in the cells receive from the spleen in the form of an "internal secretion" the agent with which to elaborate the active proteolytic ferment trypsin, which passes forthwith into the glandular ducts.

The blood supplies the vehicle by which this product of the spleen is transported to the pancreas (Herzen). It appears to be carried by the solid elements of the blood, since serum does not contain it; if carried by the plasma it is destroyed by coagulation. I find, in agreement with Herzen, that the pancreas of a dog deprived of its spleen exists in a condition of complete and permanent atrypsia; the elaboration of zymogen is excreted as such, and if it becomes subsequently changed so as to be of service to the organism, this process is carried on outside the pancreas and occurs as the result of some agency other than the spleen.

In addition, he devoted himself to the experimental proof of the recent statement of Professor Panlow, that the mucous membrane of the small intestine possesses a function like that of the spleen. He found that the mucous membrane of the small intestine furnishes a product possessing the property of converting the pancreatic zymogen into trypsin. This product is especially plentiful in the jejunum, it is

[1] Journal of Physiology, 1901, xxvii., 4 and 5, p. 323.

elaborated quite independently of the spleen, and its presence is manifest throughout the whole digestive cycle, as well in spleenless as in normal animals.

A Note on the Influence of Heat on Enzymes. Beebe[1] says the influence of variations in temperature on the reactions brought about by enzymes has long been recognized. Recently, Pozerski and Henri have attempted to demonstrate that the inverting power of the invertion of beer yeast may be distinctly augmented by heating a solution of the enzyme to about 40° C. It is necessary to raise the temperature of the solution for a short time only, in order to observe this modification; and the authors assume a change in the physical state of the solution. Observations like those described may, if verified, lead to important theoretical conclusions regarding the colloidal solutions in which enzymes occur. In his study of the pipase of blood serum, Hanriot has failed to observe similar variations resulting from changed temperature conditions. In view of the importance of the subject the writer has attempted, at Professor Mendel's suggestion, to repeat the experiments with invertin. The results have been practically negative in every case, the differences obtained with the previously heated enzyme solutions being minimal and variable, as the protocols indicate. A few experiments with amylolytic enzymes resulted similarly.

Concerning the Absorption of Fat. It is well known now that fats during the digestive act are sooner or later brought into a state of solution. This has been attributed to the action of different enzymes or ferments by which the fats are split into glycerin soluble in water and into fatty acids insoluble in water. These acids, however, combine with the sodium of the carbonated and biliary salts of the digestive juices and form soaps which are soluble in water. The fatty acids are also soluble in bile. That this explanation is the correct one for the preparation and absorption of all fats has been decided by several investigators, especially by Immanuel Munk, who asserts that there is not enough alkali for the entire saponification of the fat, and that the solubility of the fatty acids is not sufficient to account for the actual amount of the fat absorbed. Pfluger[2] in a recent paper endeavors to show the invalidity of these objections. He assumes that the ever-present carbonic acid of the cells of the mucous membrane unites at once with the alkali that is set free after the soaps have been absorbed by the cells and been decomposed again into alkali and fatty acids, the latter combining at once with the glycerin to form new fat. This newly-formed sodium carbonate is quickly absorbed by the vessels and brought back again to furnish new alkali for glands of the intes-

[1] American Journal of Physiology, 1902, vii., 3, p. 295.
[2] Archiv f. d. ges. Physiologie, Band lxxxvi., S. 1.

tinal mucous membrane and for the liver and pancreas. The alkali thus makes a constant cycle. This article concludes with a résumé of the quantitative results of his experiments which substantiate this view.

In a subsequent paper Pfluger[1] shows the power of bile mixtures to dissolve fatty acids, and states that in this respect there are great differences which depend upon the nature and the proportion of the fatty acid to be dissolved; for, while of mixtures of equal parts of oleic and stearic acids about 15 parts are brought into a form soluble in water by 100 parts of bile, in the presence of the equivalent amount of sodium carbonate this value at once goes up to 19 parts if a mixture of equal parts of oleic acid and palmitic acid is employed. Pfluger believes in view of these and other results that there are no longer any difficulties for the view that all fat is absorbed in a soluble form. He finally lays great stress on the dissolving power of bile for the fatty acids, on the fact discovered by him that the fatty acids are dissolved in bile mixtures because they are brought into water-soluble compounds which, however, are in hydrolytic dissociation. In a later paper in the same journal Pfluger concludes that in the present state of our knowledge it appears that the fatty acids are absorbed as unstable compounds. This is a condition between freedom and chemical union. The absorbability of the fats, however, presuppose their cleavage into fatty acids and glycerin.

An Investigation as to the Amount of Absorption from the Large and Small Intestine. With a view of determining their relative absorbing power, Reach[2] included a part of the large and small intestine between two ligatures and introduced the substances to be taken into these parts of the intestinal tract. The animals experimented on were frogs. From many experiments he concludes as follows: The absorption of the nutritive substances employed in these investigations is considerably less from the large than the small intestine. Gelatin solution is less readily absorbed from the large intestine than albumose solution. The addition of sodium chloride 0.7 per cent. increases the absorption of the gelatin and makes it almost equal to that of the albumose. The addition of the sodium chloride, however, to the albumose solution causes irritation of the mucous membrane, in consequence of which absorption sometimes is almost entirely stopped. In the small intestine gelatin solution is absorbed more readily than albumose solution. The addition of sodium chloride does not change the rate of absorption of gelatin, but does cause irritation with albumose. The author suggests, therefore, that an addition of gelatin and salt to nutritive enemata (for example in the form of soups rich in gelatin),

[1] Archiv f. d. ges. Physiologie, Band lxxxviii., S. 299.
[2] Ibid., Band lxxxvi., S. 247.

perhaps, may replace with advantage the usual addition of peptone preparations. This ought to be tested clinically.

The Permeability of the Intestinal Wall for Substances of High Molecular Weight. Dr. Friedenthal[1] conducted a series of investigations on rabbits, with a view of determining the permeability of the intestinal wall for colloid bodies. He found that traces of colloid substances pass through the wall, even when the organism possesses no ferment for the cleavage of the experimental substance. The smallness of the amount which passes through corresponds to the slight power of diffusion of the substance, which is an argument, in the author's opinion, for the absence of vital forces in the intestinal epithelia.

How Does the Alimentary Tract Protect Itself from Injury by Sharp Foreign Bodies. The solution of this interesting question is given by Exner[2] as follows: The stomach and intestines of the mammals operated on possess, in the muscularis mucosæ with its extension, an apparatus which is able to protect the mucous membrane from injury by sharp foreign bodies. This is effected by the formation of a dimple in that portion of the mucous membrane which is touched by the sharp object; that is, the mucous membrane recedes from the dangerous point, and, therefore, will only touch the foreign body where a contact is possible without danger. Besides, the intestines possess the faculty of bringing pointed foreign bodies into such a position that their migration through the digestive tract reduces the danger of an injury to a minimal value. If, however, a lesion of the mucous membrane takes place the hemorrhage is limited.

The Movements of the Intestines Studied by Means of the Roentgen Rays. In a well-written paper on the movements of the intestines studied by means of the Roentgen rays, which must be read to be appreciated, because the abstract leaves the impression of too broad conclusions, Cannon[3] shows that bismuth subnitrate, 10 per cent. to 33 per cent., mixed with the food renders the movements of the intestinal contents, and thereby the movements of the intestinal walls, visible on the fluorescent screen. The activity most commonly seen in the small intestine is the simultaneous division of the food in a coil into small segments, and a rhythmic repetition of the segmentation each time applied to the new segments, formed from parts of those just divided. In the cat this rhythmic segmentation may proceed at the rate of thirty divisions per minute. The effects of the constrictions causing the segmentation are: the mixing of the food and the digestive juices, the bringing of the digested food into contact with

[1] Archiv f. Physiologie, 1902, S. 149.
[2] Archiv f. d. ges. Physiologie, Band lxxxix., S. 253.
[3] American Journal of Physiology, 1902, vi., 5, p. 251.

the absorbing mechanisms and the emptying of the venous and lymphatic radicles of their contents by compression of the intestinal wall.

Peristalsis is usually combined with segmentation. As the food is advancing, interfering constrictions often separate the rear end of the mass from the main body. The separation is momentary, however; the rear end is swept into union with the main body again, and the whole mass is pushed onward until another constriction repeats the changes.

The ileocæcal valve is thoroughly competent for food entering the colon from the ileum.

The usual movement of the transverse and ascending colon and the cæcum is an antiperistalsis. This recurs in periods about every fifteen minutes, and each period lasts commonly about five minutes; the waves recur during a period at the rate usually of eleven waves in two minutes.

This antiperistalsis gives new significance to the ileocæcal valve, for the food, now in a closed sac, is thoroughly churned and mixed by the constrictions running toward the cæcum, and again exposed to absorbing walls without any interference with the processes in the small intestine.

As soon as new food enters the large intestine a strong general contraction takes place along the cæcum and ascending colon, forcing some of the food onward; a moment later antiperistaltic waves begin to pass.

With the accumulation of material in the transverse colon, deep tonic constrictions appear one after another and carry the material into the descending colon, leaving the transverse and ascending portions free for the antiperistaltic waves.

In emptying the large intestine the material in the lower descending colon is first carried out by combined peristalsis and pressure of abdominal muscles; the remainder of the material is then spread into the evacuated region, and this region is again cleared; the second remainder may be similarly affected. In normal life the new food arriving in the colon must force forward the old contents of the ascending and transverse colon.

The observations have revealed no evidence of antiperistalsis in the small intestine; but, since the ileocæcal valve will allow nutrient material under pressure to pass backward, the antiperistalsis of the large intestine may force into the small intestine a considerable portion of a large nutrient enema. Segmentation in the small intestine affects such an enema precisely as it affects food which has passed normally through the stomach.

Signs of emotion, such as fear, distress, or rage, are accompanied by a total cessation of the movements of both large and small intestines. The movements continue in the cat both during sleep and at night.

BLOOD, CIRCULATION, AND RESPIRATION.

The Formation of Blood in the Air Balloon. Justus Gaule[1] reports the results of his observations on the production of erythrocytes at high altitudes. At a height of 4200 metres he found their number increased to 8,160,000, but at the end of twenty-four hours they had so rapidly diminished that the normal number was regained. He proves by his experiments that this increase is not apparent only and due to mechanical conditions in the chamber of the hæmocytometer, as has been asserted by Schroder, but that there is an absolute increase due to an adoption of the system to the changed surroundings.

Changes in the Blood after Interruption of the Lymph Flow. Biedl and Decastello[2] report the results of some expeirments, the object of which was to determine the effect on the corpuscular content of the blood by the prevention of the lymph flow into it, either by ligation of the thoracic duct or by the construction of a lymph fistula. They found that both procedures produced but a temporary diminution in the number of lymphocytes. Even the simultaneous extirpation of the spleen in the dog could not bring on a total disappearance of the lymphocytes. They conclude with Pohl that at least during the leucocytosis of digestion a part of the lymphocytes, indeed a considerable part, enters the blood directly from the lymphatic glands. The eosinophile cells, however, in decided contrast to the polynuclear neutrophile leucocytes, showed very soon a decided decrease after the operation.

The Mutual Dependence of Irritability, Contractility, and Conductivity of the Cardiac Muscle Fibres. In a critical review of all the experimental work done with a view of solving the relationship of these three properties, H. E. Hering[3] concludes as follows: The assumption of a mutual independence of the irritability, contractility, and the conductivity of the cardiac muscle fibres is entirely without positive proof. We know, however, that the cardiac muscle may or may not show at the same time all these three properties. In consideration of the want of proof for their independence, and in consideration of the usual occurrence of simultaneous changes in the same direction of the three properties, we may accept the view of their mutual dependence.

If we consider that at the bottom of the terms irritability, contractility, and conductivity there lies one and the same property of the muscle fibres which, for its formed distinction, we may simply call its ability to react (reactions fahigkeit), the conception as to the function

[1] Archiv f. d. ges. Physiologie, Band lxxxix., S. 119.
[2] Ibid., Band lxxxvi., S. 259. [3] Ibid., S. 533.

of the cardiac muscle is much simplified. The maximal reaction of the cardiac muscle is true not only for the contractility, but also, as is well known, for the conductivity.

The power of the same fibres to react changes only quantitatively—*i. e.*, can undergo only an increase or decrease. Even under the influence of the extracardiac heart nerves the power of the cardiac muscle to react changes only quantitatively; for this it is necessary to postulate the existence of two kinds of nerve fibres.

The myogenic irregularities of the heart may be distinguished from each other as myoerethic or myodyserethic, according as they may be reduced to an increase or a decrease in the power of certain parts of the heart muscle to react. In the same way the neurogenic irregularities may be divided into neuroerethic and neurodyserethic.

The Invigorating Power of Alkali Saccharate and Alkali Fruchtosate Solution upon Isolated Hearts. A. Schucking[1] communicates the results of a series of experiments as to the sustaining power of various solutions made with the hearts of different animals, as frogs, toads, turtles, rabbits, cats, and pigs. His conclusions are as follows:

In the hearts of the cold-blooded animals which were examined there exists a system of capillary clefts, which, as in the capillaries of the warm-blooded animals, a portion of blood is retained. Even after the frog's heart is washed, for many hours blood corpuscles may yet be seen in the clefts. From the capillaries of the coronary circulation of the mammalian heart it is even more difficult to remove the last corpuscles or remnants of plasma.

Serum in high dilution, up to one-twenty-fourth, will maintain the contractility if it is kept in good condition by favorable saline solutions.

But far better than the saline solutions thus far employed is alkali saccharate with physiological salt solution—*e. g.*, 0.25 to 0.35 pro mille calcium saccharate; 0.25 to 0.35 pro mille sodium saccharate, or 0.4 to 0.5 pro mille sodium fruchtosate. But even with these solutions the heart freed from its nutriment would become unable to work. The most important properties of a good perfusion solution are isotomy and the presence of alkaline substances capable of combining with carbonic acid. In the blood this function is fulfilled mainly by the globulin alkali compounds. Additions of sodium bicarbonate and carbonate, or of traces of sodium hydrate, cannot replace this effect of the globulin alkali compounds. Potassium affects the exhausted heart unfavorably, and should not, therefore, be used in a perfusion solution.

A most perfect substitute of the globulin alkali compounds is the alkali saccharates and fruchtosates, because they are dissociable, con-

[1] Archiv f. Physiologie, 1901, Supplement Band.

stant in solution, harmless, and easily decomposed into sugar and alkali carbonates by the carbonic acid. The observations made on the hearts of cold-blooded and warm-blooded animals have fully confirmed this view.

Stronger solutions of alkali saccharates and fruchtosates often stimulate the washed-out heart to contracture from which, however, recovery can be brought about. With a small quantity of blood the saccharates and fruchtosates frequently bring on powerful beats. Additions of fructose to the solutions of the alkali fruchtosate up to 0.2 per cent. do not influence the pulsations of the heart in cold-blooded animals. Larger additions limit the duration of the heart's contractility.

Rigor Mortis in the Heart and the State of the Cardiac Cavities after Death. Many causes have been adduced to account for the fulness of the right heart and its vessels, and the emptiness or comparative emptiness of the left side in asphyxia—*e. g.*, the greater distensibility of the right heart, the influence of violent respiratory movements and muscular spasms in determining an accumulation of blood in the great systemic veins and the right heart, an alleged strong contraction of the pulmonary arterioles opposing the discharge of blood from the right ventricle, diminished suction power of the left ventricle, etc.; also the influence of rigor mortis on the left ventricle after death, though no explanation seems to have been offered as to why the right ventricle should behave differently to the left in this respect.

According to MacWilliams,[1] most of the alleged causes may be set aside as inadequate or unessential. The greater distensibility of the right heart would naturally apply equally in cases of death from causes other than asphyxia, and would obviously not account for the left heart being nearly empty. The influence of violent respiratory movements and muscular spasms is evidently unessential, since these can be excluded by the previous administration of curare without materially altering the condition found after death. The assumed contraction of the pulmonary arterioles may be shown not to be an effective cause by evidence of various kinds (study of pressure in left auricle, etc.), and so with the diminished suction power of the left ventricle. Indeed, any cause merely leading or tending to an accumulation of blood on the right side of the heart prior to death must be an unsatisfactory explanation. For, though some discordant statements have been made on the point, it is quite certain that at death both sides of the heart are distended with blood—both auricles and ventricles. The pressure in the right and left chambers has, in his experiments, been found to be equal—usually a pressure of 25 to 40 mm. blood in the rabbit, and a somewhat higher pressure in the cat.

[1] Journal of Physiology, 1901, xxvii., 4 and 5, p. 340.

Conflicting statements have been made as to the amounts of blood in the two sides of the heart immediately after death by asphyxia. One observer gives the relative proportions on the right and left sides as two to three, while another describes a very great preponderance on the right side; in one experiment (dog) he found 16 ounces on the right side, and only 2½ ounces on the left.

In MacWilliams' experiments the amount on both sides was invariably found to be relatively large; there was always found to be more on the right side than on the left, commonly in the proportion of three to two—*e. g.*, in one rabbit 9 c.c. on the right side, and 6 c.c. on the left, etc. The greater amount of blood on the right side is evidently due to the greater distensibility of the right heart; since the pressure on the two sides is found to be equal.

After death by asphyxia rigor occurs early and strongly in the left ventricle. In the rat rigor may begin as soon as nine minutes after occlusion of the trachea, in the rabbit in twelve minutes, and in the cat in fifteen minutes —though, as a rule, the periods are much longer than these. It seems probable that the diminution or emptying of the left ventricle, described by Johnson as occurring at the end of asphyxia, may have been really due to the early onset of the contraction of rigor.

Why is the right ventricle not emptied by rigor mortis like the left? In asphyxia the right ventricle dies slowly and gradually—later than the left. Rigor comes on late, it is gradual in its onset, often markedly unequal in distribution, and relatively slight in intensity.

In the larger animals marked differences may be found in different portions of the muscular walls of the right ventricle—*e. g.*, the mesial wall may be much more rigid than the rest of the ventricle. As the force exerted in rigor is confined to the period between the beginning of the attempt to shorten and its completion, it is obvious that if different sets of fibres go into rigor at different times no considerable expulsive force can be developed, even if the contractile effort was very much stronger than it is, as a rule, in the right ventricle after asphyxia. Further, the lateness of the occurrence of rigor is unfavorable to the expulsion of blood from the cavity, on account of changes occurring in the blood itself after a time, increased adhesiveness, and subsidence of the corpuscles, coagulation, etc.

In some cases after death by asphyxia, rigor comes on much earlier than usual in the right ventricle, and is much more strongly developed. When this happens the blood is expelled just as ordinarily happens in the left ventricle, so that some time after death both ventricles are found to be almost empty.

From his series of experiments MacWilliams concludes that rigor mortis in the heart differs from that in the skeletal muscles (*a*) in some

of its characters, and (*b*) in regard to the conditions which influence its appearance and intensity. The hypothesis of a relation between the time of onset of rigor and the length of the nerves connecting the muscle with the central nervous system does not hold good in the heart. The onset of rigor in the left ventricle is attended by contraction (or retraction) of considerable force—sufficient to get up a pressure of 30 mm. Hg (in the cat) in a manometer connected with its cavity. In some cases slow minor contractions and relaxations occur after the persistent contraction of rigor is more or less fully developed.

While rigor is the chief factor in determining the post-mortem condition of the heart as regards fulness or emptiness of the different chambers, etc., the time of occurrence of coagulation of the blood, and the post-mortem intravascular pressure are also concerned.

After death there is always a positive blood pressure on both sides of the heart, and this pressure is equal on the two sides (cases of hemorrhage and mechanical interference excluded). In cases where the cardiac muscle dies very slowly and goes on discharging energy long after the circulation has ceased, rigor is commonly less strongly developed, and both ventricles may contain much blood tweny-four hours after death.

After death from paralysis of the heart induced in various ways, the state of the heart (some hours afterward) varies widely: (*a*) Both ventricles may be contracted and practically empty (morphine, etc.); (*b*) the right ventricle may be distended and the left empty—what is usually regarded as an asphyxial distribution of the blood being present (chloroform, lactic acid, ammonia), or (*c*) both ventricles may contain much blood (potassium salts, etc.).

After death by asphyxia the most common post-mortem condition is one which has long been recognized as characteristic of this condition—right side distended, left side comparatively empty. The reason for this is that the left ventricle is emptied by early and strong rigor, the right ventricle is not emptied because rigor is late in appearance and weak, and unequal in distribution, etc. But in some cases of death by asphyxia both ventricles are found contracted and empty, and in other cases both contain much blood.

After death by chloroform it is impossible to determine with certainty from the post-mortem examination of the heart whether failure of the respiration or of the heart had occurred first.

A Physiological Study of the Pulmonary Circulation. From experiments conducted by Horatio C. Wood, Jr.,[1] it seems proven that various influences, among which are asphyxia or stimulation of a sen-

[1] American Journal of Physiology, 1901, vi., 5, p. 283.

sory nerve, elevate the blood pressure in the pulmonary artery as well as in the aortic circulation. This elevation of the blood pressure is not a passive one, but is due to a direct contraction of the bloodvessel walls; for it is possible to cause a rise of pressure in the pulmonary system without a rise in the carotid pressure; and, on the other hand, an elevation of the aortic pressure does not necessitate a rise of the pulmonic pressure. Nitroglycerin and the other nitrites, while lowering greatly the general blood pressure, cause a slight elevation in the pulmonic system. Digitalis does not affect the vasomotor system of the lesser circulation as it does that of the greater, so that the rise in the carotid pressure is not accompanied by any rise in the pulmonic pressure.

CONTRIBUTIONS TO THE PHYSIOLOGY OF THE ADRENAL BODIES.

Drs. Strehl and Weiss[1] found from a series of experiments made on dogs, cats, rabbits, guinea-pigs, rats, mice, frogs, and other animals that extirpation of the adrenal bodies invariably caused death. One exception to the general rule was explained by the presence of a displaced supernumerary adrenal organ. The investigators believe that the cause of death is the absence of a substance which produces a rise of the blood pressure and normally is active in keeping it at its proper height. They further express their belief that these bodies may produce a substance which neutralizes the poisonous matters which accumulate in the blood. That the fall of the blood pressure, which occurs immediately after the extirpation of the second adrenal body, is not due to the operation as asserted by Lewandowsky, but to the absence of a body which maintains the blood pressure, was demonstrated by two experiments. In the first experiment it was shown that the cutting of the vein of an adrenal body has the same effect as the extirpation of the organ, if the other had previously been extirpated. In the second experiment it was found that clamping the vein lowered the blood pressure, while removal of the clamp was followed by a rise of the pressure even temporarily above the normal level.

The Physiological Action of Extracts of the Suprarenal Bodies. From a series of observations on cats, Langley[2] states the following as the physiological action of extracts of the suprarenal bodies:

Suprarenal extract causes a brief but active secretion from the salivary and lacrymal glands, and this is unaffected by degeneration of

[1] Archiv f. d. ges. Physiologie, Band lxxxvi., S. 107.
[2] Journal of Physiology, 1901, xxvii., 3, p. 37.

the post-ganglionic fibres of the superior cervical ganglion. It will cause a secretion from the submaxillary gland after atropine has been given in sufficient quantity to paralyze the chorda tympani, and the secretion occurring is increased by stimulation of the chorda tympani. But after a large dose of atropine, injection of suprarenal extract into a vein does not cause a secretion. Apparently there is a mutual antagonism between the two substances. It causes a primary moderate pallor of the gland, followed by a moderate flushing, and these effects are obtained after degeneration of the post-ganglionic fibres of the superior cervical ganglion. It causes also some secretion from the mucous membranes, an increase followed by a decrease in the flow of bile, possibly in consequence of variations in blood pressure and blood flow; it does not cause secretion from the pancreas if this gland is not secreting at the time, but it may increase a secretion already going on; it apparently does not cause secretion from the sweat glands of the foot of the cat.

The extract, as shown by Boruttau, causes inhibition of the intestine, and, as shown by Lewandowsky, it causes inhibition of the urinary bladder. It causes also inhibition of the cardiac sphincter of the stomach, the stomach itself, and of the gall-bladder.

It causes in the cat, as shown by Lewandowsky, dilatation of the pupil, protrusion of the eye, retraction of the nictitating membrane, and separation of the eyelids, and, as also shown by Lewandowsky, these effects are produced after degeneration of the post-ganglionic fibres of the superior cervical ganglion. They are not prevented by ligature of the short ciliary nerves. In the dog the extract, however, may cause slow contraction of the pupil, with little or no other eye effects; the cause of the contraction has not been determined.

It causes contraction and pallor of the uterus, vas deferens, seminal vesicles, etc.; the contraction being especially marked in the rabbit.

As shown by Lewandowsky, it causes contraction of the muscles of the hairs, but the effect is slight compared with the effects mentioned above, and with moderate doses is often absent. It causes dilatation with pallor of the end of the rectum and internal sphincter in the rabbit, and slight contraction with great pallor in the cat and dog.

Its action on the arteries is unequal, it acts relatively more on the medium-sized arteries of the abdominal viscera than on the small but easily visible ones in the viscera (save the spleen), but it causes great constriction of very small vessels, either arterioles or capillaries. It has a comparatively slight action on the vessels of the bladder. It causes great contraction of both large and small subcutaneous arteries. That Oliver and Schafer, Szymonowicz and Cybulski, and others have observed general contraction of bloodvessels and rise of blood pressure

hardly needs mention. The extract does not appear to cause any contraction in the general veins of the body.

It does not cause any marked contraction of the tunica dartos of the scrotum (cat), but it may, perhaps, have a trivial effect.

THE EYE.

The Behavior of Accommodation during Stereoscopic Vision. In using the stereoscope, Dr. O. Weiss[1] found that when the vision was directed from a far to a near point on the picture, he experienced a strain of his accommodation. By objective methods he discovered that during the transference of the vision there was a bulging forward of the pupillary margin and the anterior surface of the lens. The study of the catoptric images of the anterior surface of the lens also confirmed his view.

It was found, however, that the effort of accommodation was much greater than was required for the slight amount of convergence necessary to direct both eyes from a point in the background to a point in the foreground of the picture. To explain this the author assumes that the impulse brought about by the idea of some bodily object extends to convergence as well as accommodation, but that the muscular movement of convergence is much more rapidly controlled than that of accommodation. This surplus of accommodation is given up very quickly, so that very few people observe that the image of an object in the foreground at first appears blurred.

Table Showing the Increase of Curvature of the Anterior Surface of the Crystalline Lens Necessary for Accommodation at Different Distances. In connection with his experiments on stereoscopic vision, Dr. Weiss had occasion to ask what must be the curvatures of the anterior surface of the lens in order to enable the eye to be in focus at different distances. He assumed for the calculations that the changes in the length of the radius for the anterior surface and for the posterior surface and for the thickness of the lens are in a constant ratio. His published results[2] are given in the following table:

[1] Archiv f. d. ges. Physiologie, Band lxxxviii., S. 91. [2] Ibid.

Radius of the anterior crystalline surface in mm.	Distance of the object for which the eye is accommodated in mm.	Radius of the anterior crystalline surface in mm.	Distance of the object for which the eye is accommodated in mm.
10.0	Infinity	7.9	318
9.9	8150	7.8	300
9.8	4037	7.7	283
9.7	2668	7.6	268
9.6	1983	7.5	255
9.5	1572	7.4	242
9.4	1298	7.3	230
9.3	1102	7.2	219
9.2	955	7.1	209
9.1	841	7.0	199
9.0	749	6.9	190
8.9	674	6.8	182
8.8	612	6.7	174
8.7	559	6.6	167
8.6	514	6.5	160
8.5	475	6.4	153
8.4	440	6.3	147
8.3	410	6.2	141
8.2	383	6.1	135
8.1	359	6.0	130
8.0	337	0.0	000

The Visibility of the Roentgen Rays. It was observed by Roentgen that if he passed a vertical metal slit from right to left between eye and tube a luminous line was seen which had at first a curved, then a straight, and finally again a curved form, the curvature being opposite to the first. Coral, Levy-Dorn, and other experimenters did not succeed in verifying this observation.

Dr. Crzellitzer[1] has repeated and enlarged upon these experiments, and was enabled to confirm for his eyes the statements of Roentgen, and found that the phenomenon could not be explained by assuming efflorescence of the cornea or lens. He further found that the macular region showed no special sensibility to the Roentgen rays, but that such was shown by the equatorial region of the retina, which produced a beautiful light circle. In a note he refers to the work of F. Himsted and W. A. Nagel, who have made it appear very probable that the Röentgen rays stimulate only the rods of the retina.

THE MOVEMENTS OF ACCOMMODATION IN THE HUMAN EAR.

The view of Mach, published in 1863, that the muscles of the middle ear acted somewhat like the ciliary muscle in the eye, viz. : that they regulate the tension of the drum membrane and other parts in such a

[1] Archiv f. Physiologie, 1902, S. 156.

way as to enable them best to respond to different tones, has come up for consideration by Henson.[1] He offers the following experiment which, he believes, proves that the observed sensations depend upon movements of accommodation. If a tuning-fork (of 400 to 1000 vibrations) attached to a sounding-box is made to vibrate, and if at the same time a metronome is made to tick (40 to 60 times per minute), one can hear very shortly after the metronome tick an increase and then a decrease in the tuning-fork tone. If the metronome be stopped, the tuning-fork tone remains very uniform. If the velocity of the metronome is increased to about 200 ticks per minute, the variations of the tuning-fork tones become indistinct, but occasionally may be heard. The process of accommodation, therefore, takes place very slowly, requiring about 0.3 second for its full development. He recommends the experiment to otologists, and admits that the whole question needs further elucidation.

THE MUTUAL ANTAGONISM OF CURARA AND PHYSOSTIGMINE.

A discovery of the greatest practical as well as scientific interest was made by Rothberger, viz.: that physostigmine was a quickly acting antagonist to curara. From a series of experiments on mammals the author draws the following conclusions:[2]

Between curara and physostigmine there exists a double antagonism. Muscles of an animal paralyzed by curara regain their excitability, as shown by indirect stimulation, a few seconds after the injection of physostigmine. Muscles which are the last to be paralyzed by curara are the first to regain their excitability after the injection of physostigmine. This latter drug has the same point of attack as the former. The effect of the physostigmine injection is independent of the duration of the curara paralysis.

If a mixture of these two drugs be injected into the vessels of an animal, there is at first a marked curara paralysis, which is succeeded by a spontaneous return of activity in about one-half hour.

Physostigmine may, therefore, be regarded as a physiological antagonist to curara.

[1] Archiv f. d. ges. Physiologie, Band lxxxvii., S. 255.

[2] Ibid., S. 117.

HYGIENE.

By CHARLES HARRINGTON, M.D.

WATER.

While no single factor has added greatly to the subject of hygiene during the past year, the advances have been interesting and important.

Purification of Water. According to Hünerman and Doiter, sodium hypochlorite, employed to an extent sufficient to yield 40 milligrammes of effective chlorine to each litre of water, will destroy all typhoid fever and cholera organisms and B. coli communis in ten minutes. The sodium compound is more efficient than chlorinated lime, since the whole of its available chlorine is diffused almost instantly through the water and acts at once. After purification, the chlorine is neutralized by the addition of 140 parts of sodium sulphite to each 40 parts of chlorine. If the amounts of the different compounds added are most carefully determined, the water is practically unaltered in appearance, taste, smell, and hardness at the conclusion of the process. Purification by means of bromine, according to the process of Schumburg, has been given a fair practical test by Schüder,[1] who reports it as unreliable and unpractical.

Poisoning by Water Contaminated by Zinc Compounds. A somewhat extensive outbreak of poisoning by water contaminated by zinc through storage in a galvanized iron tank has been reported by Gimlette.[2] Of fifty-six consumers thereof forty-three were attacked with gastro-intestinal disturbance, the symptoms being colicky pains, diarrhœa with consequent anæmia and emaciation, and a spurious form of dysentery.

Growth of Bacteria through Porcelain Filters. It has been accepted generally that ordinary water bacteria can grow through the lacunar spaces of porcelain filters in a few days' time, but that the pathogenic species, which gain access through contamination by sewage, cannot multiply, because of the absence of conditions essential to their growth. Some observers have held that the chief obstacle is a lack of suitable nutrient material, and that the addition of broth will remove it.

[1] Zeitschrift f. Hygiene u. Infektionskrankheiten, 1901, xxxvii. p. 307.
[2] British Medical Journal, September 7, 1901.

Contradictory results, published by a number of investigators, led Major W. H. Horrocks[1] to reinvestigate the subject, using Chamberland-Pasteur and Berkefeld filters. Broth, sterilized sewage, sterilized dilute sewage, sterilized ditch water, and sterilized drinking water, all inoculated with B. typhosus, were used in making the tests. With the Berkefeld bougies, the results were uniformly positive, the organisms appearing as early as the fifth day and at latest on the eleventh. The bougies were then cleaned by brushing or by boiling and then were further tested. The one cleaned by brushing yielded the bacillus; the other, as was to be expected, gave negative results. The same tests made with the Chamberland-Pasteur candles gave negative results in every case, even after three weeks. The difference in results is attributed to the larger size of the lacunar spaces, and to the consequently diminished immobilizing and devitalizing influences. The Pasteur filter, with proper care to prevent direct passage through flaws or imperfections, ought, therefore, to give perfect protection against water-borne typhoid; but the Berkefeld filter should be sterilized in boiling water at intervals of three days, in order that the bacteria which have already penetrated shall be destroyed.

The Significance of B. Coli Communis in Drinking Water. Houston,[2] agreeing with the majority of bacteriologists, insists upon the importance of attention to the relative abundance of B. coli communis and other sewage organisms in deciding whether or not a given water is potable, but it is difficult to decide what volume of water yielding the typical organisms shall be considered as indicative of probable sewage contamination. Water contaminated by one part of sewage in 100,000 will show the organisms after two months' storage, if 200 c.c. are employed in the test, and, therefore, he would say "that a water which contained B. coli so sparsely that 200 c.c. required to be tested in order to find it, had probably been polluted with sewage, but the contamination was not of recent date."

W. G. Savage,[3] in an interesting article on this subject, quotes Jordan as objecting to B. coli as a true index of sewage contamination, because it may be found in spring water beyond any suspicion of contamination. He quotes, also, Theobald Smith, who says that it is safe to infer that an organism like B. coli in water means contamination, and also Weisenfeld, Horrocks and Pakes. Savage believes that it is not so much the presence of B. coli which is of positive value as the number present; that the kind of water in which this organism is found is of great importance; that a number of bacilli per litre may be passed

[1] British Medical Journal, 1901, p. 1471.
[2] Ibid., December 21, 1901.
[3] Journal of Hygiene, July, 1902, p. 320.

as safe, or at least as no evidence of danger of contamination, in water from one source, which would be sufficient to condemn water from another; and that the exact point of the water-supply from which the sample is collected is of great importance. Frequently, results differing considerably are obtained with samples taken from source and tap, respectively, and with arbitrary standards one would be condemned and the other passed. His conclusions are as follows:

1. In estimating the significance of B. coli in a sample of water, the particular kind of water must be carefully considered; also the exact part of the system from which the sample was taken.

2. The number of B. coli present is an essential factor, but arbitrary standards of the number of this organism allowable per litre are of but little value and are fraught with considerable possibilities of error, unless the particular kind of water and the local conditions are considered in every case.

3. Waters which show no B. coli in 50 c.c. are of a high degree of purity, and, therefore, the proved absence of this organism in this amount, and, still better, in larger quantities, is of great value.

4. B. coli should be absent from at least 50 c.c. of spring water; possibly from greater amounts.

5. In upland surface waters, the presence of B. coli in 40, 10, or even 2 or 1 c.c. means contamination, but not necessarily a contamination which it is essential to prevent. It may be from contamination with the excreta of animals grazing on the gathering areas, and is by no means necessarily from sewage or other material containing specific organisms of infection. Further, there is no evidence that an amount of such animal contamination sufficient to cause a considerable number of B. coli per litre to be present in the water is harmful.

If B. coli are present in numbers greater than, say, 500 per litre (or even in that amount), such a water is suspicious, as it is rare to get so many B. coli in a water purely from the kind of animal contamination indicated, and further investigation is desirable. In filtered samples, the number of B. coli is, as a rule, considerably reduced.

6. Chemical analysis cannot be considered a delicate method of detecting organic contamination, because it may fail with many waters in which pollution is undoubtedly taking place.

7. In surface wells, B. coli in large numbers indicate a surface or other contamination, generally very undesirable if not actually dangerous. A knowledge of the position and the possibilities of contamination is very desirable in giving an opinion as to the purity of the water.

Neutral Red as a Means of Detecting Bacillus Coli in Water. It has been found by several investigators that media containing neutral red are changed in color to canary yellow by B. coli communis, but not

by B. typhosus. The reaction was found to be constant in an investigation of a large number of races of the organism, but it was shown also that it is brought about by certain other bacteria, including B. tetani, B. œdematis maligni, B. enteritidis, and B. anthracis symptomatici. The majority of aërobic pathogenic bacteria have been tested, with negative results. In order to ascertain whether the reaction affords a rapid means of detecting B. coli in water and of estimating the number present, R. H. Makgill[1] conducted a series of experiments, which led to the conclusion that a water which, within forty-eight hours, produces a typical canary yellow in neutral-red media, which change of color is accompanied, when glucose-agar is used, by green fluorescence and gas formation, may be considered to contain B. coli. He found that B. tetani and B. œdematis maligni produce the same appearance as B. coli in glucose-agar, even when the surface of the medium is exposed to the air, but in bouillon the anaërobes produce the reaction only when oxygen is excluded. B. mesentericus was found to change the red to a dull orange, both in bouillon and glucose-agar.

In bouillon, a reaction was obtained in every instance within twenty-four hours, even with dilutions containing from one to five organisms per cubic centimetre. In extreme dilutions, the reaction did not extend to the surface of the fluid within twenty-four hours, and the lower portion had a more orange tint than when the organism was plentiful. With numerous bacilli present, the reaction occurred within twelve hours.

W. G. Savage[2] found that it is not a matter of indifference what strength of glucose and of neutral red is used, and that, if an excessive amount of the latter be added, it may not be reduced. To determine whether B. coli will always give the reaction, and whether it is the only organism which, under the conditions of the test, will give the reaction, he instituted a series of experiments, from which he concluded that, while a positive reaction is not absolutely diagnostic of B. coli, in the vast majority of cases it points to its presence; that, while a negative reaction does not absolutely exclude the organism, it makes its presence highly improbable; and that the test is very easy of application and of great value in the routine examination of water.

Methods of applying the test are given also by Ernest E. Irons[3] and by Savage[4] in another paper.

MILK.

Improvement in Milk Supplies. It is gratifying to notice the widespread increase in interest on the part of public health authorities

[1] Journal of Hygiene, 1901, p. 430.
[2] Ibid., 1902, p. 437.
[3] Ibid., July, 1902, p. 314.
[4] Public Health, May, 1902, p. 485.

in this country and elsewhere in the character of the milk-supply. Until within very recent years, where laws regulating the sale of milk have been enforced, the object has been chiefly the prevention of fraud on the part of the producer, middleman, and retailer; in other words, the enforcement of a police regulation rather than of a sanitary measure. It is true that great injury to consumers, especially to those in early life, may be caused by the substitution of volume for substance, particularly if the water employed for the purpose of extending milk is derived from a polluted source. Robbing the milk of its cream and concealing the fact, so far as the outward appearance is concerned, by the admixture of coloring agents, such as annotto and aniline orange, may also work injury as well as injustice; and the same is true of the practice of preserving it with borax, boric acid, and formaldehyde. But there can be no doubt that milk of the best quality, so far as richness in normal constituents is concerned, may be equally or more harmful if it is swarming with ordinary non-pathogenic bacteria; for among the common saprophytes are many species which exert a peptonizing action on the proteids, and elaborate powerful toxins which play a great part in the causation of the severe gastro-intestinal disturbances of infancy and of early childhood.

The attention of sanitarians is now being drawn fully as much to the necessity of excluding these organisms and preventing the extensive multiplication of those unavoidably present, as to the importance of preventing fraudulent manipulation. The most striking evidence of inexcusable, widespread carelessness in methods of procuring and handling milk, and of the comparative ease with which milk can be marketed in a clean state, has been given by Dr. W. H. Park,[1] of New York. In his investigations, he found that milk, drawn from cows with all reasonable care to insure cleanliness, and cooled at once to 45° F., yielded an average of 6000 bacteria per cubic centimetre at the end of five hours, and showed a striking diminution at the end of twenty-four hours, but an increase after a further period of like duration. Milk drawn in cold weather in fairly clean, well-ventilated, though dusty, barns, by milkers whose hands were wiped off, but not washed, from cows whose udders were cleansed so far as visible dirt was concerned, yielded, at the time of milking, 15,500 bacteria per cubic centimetre; after twenty-four hours, 21,666; and after forty-eight hours, 76,000. In this case, the milk was cooled within two hours to 45° F. Milk drawn in winter under the conditions of cleanliness or uncleanliness that obtain in the average country barn, and by the usual methods, yielded, shortly after milking, after twenty-four hours, and after forty-eight hours, respectively, 16,650, 31,000, and 210,000 bacteria per

[1] Journal of Hygiene, 1901, p. 391.

cubic centimetre; and in summer, after like periods, respectively, 30,366, 48,000, and 680,000. Twenty specimens of average milk, taken immediately on arrival in the city, some from a distance of more than 200 miles, yielded from 52,000 to no less than 35,200,000 (average 5,669,850) bacteria per cubic centimetre. The average temperature of the cans from which the specimens were taken was 45° F. Park noted that milk which is rapidly cooled to the proper extent keeps almost unaltered for thirty-six hours, but otherwise it deteriorates rapidly. He showed the influence of different temperatures on the rapidity of bacterial multiplication by allowing portions of the same specimen to stand under otherwise similar conditions. Below 50° F., there was, at the end of twenty-four hours, no increase, but a decrease, in number. At higher temperatures, the rate of multiplication was enormous. Beginning with 3000 bacteria per cubic centimetre, the number increased after twenty-four hours' exposure to 60° F., to 180,000; to 68° F., to 450,000; to 86° F., to 1,400,000,000; and to 94° F., to 25,000,000,000 per cubic centimetre.

For the avoidance of rapid deterioration of milk through bacterial multiplication, the means are simple. They include cleanliness everywhere—of the stable, of the milkers and their clothing, of the milk-pails and other vessels, of the cow's exterior—and low temperatures. The question arises, How may these conditions be secured? They may be secured by a process of education (compulsory for the majority) of milk producers. Park advocates a bacterial standard for milk on arrival at the city, and it seems reasonable to conclude that a farmer after having his milk refused a number of times will, for his own protection, adopt methods to secure a cleanly product. A standard of not exceeding 500,000 bacteria per cubic centimetre is suggested. This appears unnecessarily high, but it is probable that when one adopts measures to keep within this limit, the number of bacteria will be found to be very much lower than the permissible maximum, and in the end the producer will find that extreme care will bring more substantial pecuniary reward than will only moderate attention.

The conditions found by Park to exist in New York are, of course, not peculiar to the milk-supply of that city, but probably obtain almost universally.

In addition to the common species of non-pathogenic bacteria, it has been shown by Lameris and Van Harrevelt, Escherich, Adametz, Eastes, Bergey, Leblanc, Reed and Ward, and others that milk from apparently healthy cows may contain streptococci and staphylococci in great numbers. Reed and Ward[1] have reported that an apparently

[1] Centralblatt f. Bakteriologie, etc., 1901, p. 496.

perfectly healthy cow of the Cornell University herd yielded streptococci at intervals for more than two and a half years. When she was killed the udder showed them in abundance.

As an example of what can be done to insure an ideal milk-supply, the following may be cited: According to an editorial in the *Philadelphia Medical Journal* (June 7, 1902), the term "certified milk" originated in New Jersey, in 1893, with the Essex County Medical Commission, which was organized for furnishing milk, properly prepared and properly handled, suitable for clinical purposes. The eighteenth annual report of the Commission demonstrates how stringently the dairyman with whom the contract was made nine years ago has adhered to the standard required. The milk contains not large numbers of micro-organisms, and is absolutely free from pathogenic species; it may be kept, under ordinary conditions, without souring for a long time. The Commission employs a chemist, a bacteriologist, and three veterinarians. The farm buildings are well constructed, well drained, and well ventilated. The feed is of exceptional quality, and is kept apart from all sources of contamination. The water-supply is good, and everything is kept scrupulously clean. No other live-stock of any sort and no sick cows are kept on the place. The stables are cleaned so frequently that no animal odors are noticed. The cows are milked in clean buildings by clean milkers in clean overalls, and the process is not begun until the udders have been cleansed. The milk is transferred at once to sterile dry cans, after passage through a strainer having no less than 100 meshes to the linear inch. It is cooled in a separate building to between 40° F. and 50° F. within three-quarters of an hour after milking; it is placed in glass jars which have been cleaned and sterilized, and then they are hermetically sealed, and are ready for shipment.

Shall Milk be Sterilized? The question whether milk should be boiled in order that the contained bacteria may be destroyed is discussed by Ransom,[1] who concludes that there is no incontrovertible evidence to show that pasteurized milk, or even milk which has been boiled for ten or fifteen minutes, loses at all in nutritive properties, and that it is not probable that it can cause infantile scurvy if it is consumed within twenty-four hours. Pasteurization is more difficult to carry out than boiling and is less reliable; so, in times of epidemics of summer diarrhœa, Ransom holds that the heating should be prolonged for at least a half hour, and if not consumed within a few hours, the milk should be boiled again, since the spores of B. sporogenes enteritidis are very resistant.

[1] British Medical Journal, February 22, 1902.

Opposed to Ransom's views is the fact that many cases of scorbutus and dyspepsia have been observed in infants fed with sterilized milk, no other explanation being offered. It seems not unlikely that the conditions are connected with the destruction of the zymases present in normal milk. These ferments have been studied by Spolverini,[1] who isolated seven different kinds, none of which can withstand the temperature to which milk must be heated in the process of sterilization.

Tuberculosis and Infected Milk. In spite of the promulgation of Koch's statement concerning the uselessness, so far as human life is concerned, of attempting to restrict the spread of tuberculosis among dairy cattle, the subject of danger of transmission of tuberculosis through infected milk is more interesting than ever, and much literature on the subject has been called forth; but, it must be said, the weight of clinical evidence is against those who believe such infected milk to be the cause of a large percentage of deaths from tuberculosis among children. Indeed, Dr. D. Bovaird[2] asserts that it is only in England that numerous cases of primary intestinal tuberculosis are reported, and that it is a very rare condition in and near New York. The rarity of primary intestinal tuberculosis is attested also by Koch, who, some time ago, called attention to its great infrequency among children in public institutions in Berlin; by Biedert,[3] who maintains that the amount of tuberculous infection through the alimentary tract is very small; by Adami,[4] who is of the opinion that peritoneal and intestinal tuberculosis are remarkably rare in the large cities of this continent; and by Crookshank,[5] who disbelieves in the theory of connection of infected milk with abdominal tuberculosis of children, and is of the opinion that insufficient consideration is given to the possibility of direct infection from human sources. Adami draws attention to the fact that during the year ended June, 1900, of 935 deaths from tuberculosis in Montreal, but 4 were of children under fourteen, and 3 of these were from abdominal tuberculosis in children under five years. Jacobi[6] admits that primary tuberculous ulcerations of the intestines and primary tuberculosis of the mesenteric glands are rare, but contends that peritoneal tuberculosis is very common.

In spite of the small number of cases offering even moderately strong evidence of causation of tuberculosis by infected milk, and notwithstanding the fact that there are marked differences between the bacilli of bovine and human tuberculosis, we cannot ignore the possi-

[1] Archives de Médecine des Enfants, December, 1901.
[2] Archives of Pediatrics, December, 1901.
[3] Berliner klin. Wochenschrift, November 25, 1901.
[4] Philadelphia Medical Journal, February 22, 1902.
[5] Lancet, November 2, 1901. [6] New York Medical Journal, January 25, 1902.

bility of danger in individual cases. Prof. Theobald Smith[1] believes that it is possible that the absorption of bovine bacilli is interfered with by some influence which permits the human bacilli to pass, and that, although racial differences appear to prevent the absorption of the bovine bacilli under the usual conditions, there may be danger if the digestive tract is flooded with bacilli from tuberculous udders. There are those who believe—as, for example, Lablanc[2]—that the danger of the milk from tuberculous cows does not reside in the contained bacilli, but in toxins which they elaborate; and Michellazzi has demonstrated that such milk injected into tuberculous animals causes a reaction similar to that produced by the employment of tuberculin, and it is held that the milk of a tuberculous mother will eventually prove toxic to her child.

A New Preparation of Milk. Victor E. Nelson, United States Consul at Bergen, under date of January 24, 1902, reports to the State Department a process, originating in Sweden, for the changing of milk into a fine flour that may again be transformed into milk through solution in water. The peculiarity of the discovery lies in the fact that the powdered dried milk can be dissolved in water, for, under ordinary conditions, the dried residue is practically insoluble therein. No description is given of the apparatus, as the inventor has applied for letters patent. The flour looks like wheat flour, and has the aroma of milk. It can be preserved in tin cans, wooden barrels, and even sacks and paper bags. One part by weight of flour is sufficient to yield ten parts of milk. The flour does not turn sour, and is not affected by changes in the weather. Samples were kept for weeks in a thermostat at blood temperature, and no change occurred.

CHEMICAL PRESERVATIVES IN FOODS.

Since the announcement by the German government of its intention to put into full effect, in October, 1902, the law prohibiting the use of preservatives in meats, much interest has been taken in the subject on both sides of the Atlantic, chiefly on economic grounds, since, if American shippers are prevented from sprinkling the exterior of meat with boric acid and borax—a process which serves to prevent the meat from becoming slimy in transit—our foreign trade in meats will be much diminished, and in Germany the consumer will pay an advanced price. To sanitarians the question is of very great importance, on account of the possible effect of these and other preservatives on the human system. The German government bases its action upon expert evidence submitted by men of the highest technical training, but it has

[1] Medical News, February 22, 1902.

[2] Lyon Médicale, 1901, p. 561.

without doubt been influenced considerably by the demands of the Agrarian party, which hopes for the exclusion of American foods. We in this country are very careless in the matter of the purity of the food-supply, and it is difficult to convince the public that small daily doses of well-known drugs, not commonly classed as poisons, can do any harm whatever, more especially since no immediate symptoms are produced. Naturally a substance which will produce violent action hardly lends itself for use as a food preservative, since attention would immediately be drawn to the food as the cause of sickness; nor could one use a substance which in a short time would cause, even in a minority of subjects, perceptible ill-effects. Those who have investigated the problem of food preservation are inclined to the belief that, since the agent is used not to benefit the consumer, but to make it possible to extend the commercial life of foods and thus to benefit the seller; and since the harmlessness of a preservative may not properly be inferred from absence of symptoms of marked character in the consumer; and since if these agents exert any injurious effects, they do so insidiously, so that the latter are not recognized as due thereto, but attributed to some other cause, it is best to be on the safe side and require either that preservatives shall not be used at all or that foods containing them shall be so labelled that the consumer shall be notified of their character, and thus may elect whether or not to subject himself to possible danger. Admitting that we do not know what effect, if any, some of the commonly used preservatives may exert, it becomes a very difficult matter to draw the line between such preservatives as shall be permitted and those which shall be prohibited. As Leffmann[1] has said, the placing of saltpetre, vinegar, salt, and wood smoke among permissible antiseptics, and designating boric acid, formaldehyde, salicylic acid, and betanaphthol as poisonous substances, is wholly arbitrary, the whole question being one of dose. Certainly, it would be difficult to explain why saltpetre, which all therapeutists know is anything but an inert drug, should be classed by legislative bodies among harmless preservatives, unless it is that its use has extended through so many years that it is now commonly so regarded.

In the preservation of fish and meats the substances commonly employed include boric acid, borax, and sodium sulphite. Other preservatives, like salicylic acid, formaldehyde, and sodium fluoride are better adapted to other kinds of perishable foods, such as milk, saccharine solutions, and fruit juices.

Boric Acid and Borax. The German Imperial Board of Health has issued a pamphlet giving the results of experiments made to deter-

[1] Philadelphia Medical Journal, June 14, 1902.

mine the action of borax. These experiments were not of the usual duration—a few days or possibly weeks—but extended over two years. It was shown that borax in the system interferes with nutrition, since it retards the assimilation of albumin and fats. The period of elimination is eight days. These results are in decided disagreement with those obtained by Tunnicliffe and Rosenheim, reported in April, 1901, and by Liebreich, in 1900, and by several others who have made recent investigations of the subject. Vaughan and Veenboer,[1] experimenting with borax on meat, found that meat not treated with borax, and kept at ordinary temperatures, becomes slimy within a few days. From the surfaces of specimens so kept, they isolated twenty different species of micro-organisms, fourteen of which were peptonizing bacteria. Inasmuch as it is the usual practice to wash meats so treated as soon as they arrive at their destination, they see no objection to this use of borax, and it would appear reasonable and proper to allow this practice, provided the preservatives do not penetrate the meat to any considerable extent. On the announcement by the German Government, Virchow, who was very strongly opposed to such action, made known that for years he had taken a daily dose of borax with apparent benefit, and that since reaching his eightieth birthday he had doubled the dose.

It has become generally conceded that, whether or not small amounts of borax and other preservatives are injurious to the system, they should be rigidly excluded from milk, since this food should be consumed in as fresh a state as possible, and because the amount of borax or boric acid, or of mixture of the two, necessary to prevent milk from souring is so large that a child in the course of a day, drinking the usual amount of milk, would receive an amount of the preservative far in excess of what is regarded as a large dose for adults in the treatment of epilepsy.

Sodium Sulphite. The most objectionable of all the chemical preservatives, the one that has fewest friends among scientists, and, at the same time, the one which is used more extensively than any other in chopped meat (Hamburg steak), is sodium sulphite. It is tolerably safe to assert that nearly every pound of the attractive looking, bright-red mounds of Hamburg steak exposed in our public markets contains this or some other salt of sulphurous acid. It apparently never occurs to the purchaser that the meat, although exposed to the air for hours at a time, retains its bright red color without changing at all, although he may be well aware that raw meat, chopped fine, in the household turns grayish very quickly. It is to preserve the color, and not to restrain putrefactive processes, that the sulphites are used. Their antiseptic

[1] American Medicine, March 15, 1902, p. 421.

properties are slight or wanting, as has been proved repeatedly. From recent work on the subject the following may be cited: Stroscher[1] examined eighteen specimens of chopped meat obtained from butchers in Leipzig, and found that sixteen contained sulphites, the content of which did not stand in inverse proportion to the number of bacteria present, as it should if the salts were true antiseptics. Indeed, it was learned that it is a common practice to add large amounts of the preservative to meat not only already rich in bacteria, but even to a certain extent already spoiled. In this way the desired red color is attained, and the fact of beginning decomposition is concealed from the purchaser. As many as 18,559,000 bacteria per gramme were found in meat prepared in the ordinary manner against less than a twentieth as many when sterile machinery was used. Stroscher concludes that sulphites in meat are objectionable because they have no antiseptic action worthy of the name; because they cause a red color which deceives the consumer so that very stale meat may be sold as fresh; and because they cause the meat to acquire properties dangerous to health. Janke,[2] too, has tested the preservative properties of sodium sulphite, and comes to about the same conclusions. He added definite amounts (0.02, 0.04, and 0.06 per cent.) of the substance to meat during the hashing process, and kept the meat so treated, some in open and some in closed dishes. It appeared that decomposition was postponed for a short time; that meat that had once gone wrong in color could not have its fresh appearance restored; that meat which had begun to smell badly continued to do so in spite of treatment; and that meat which has been treated may have a normal appearance and yet be undergoing incipient putrefaction. Sixteen samples of chopped and sliced meat were found by Eugene Mayer[3] to contain sulphurous acid in amounts ranging from 0.0291 per cent. to ten times as much. The average amount was 0.1103 per cent. All of them presented a bright-red, fresh appearance on the surface; the interior was grayish red, but became bright red on exposure to the air. Ten of the specimens showed from 1,695,000 to 471,511,000 bacteria per gramme of meat. Four samples of unchopped meat from the market yielded, after being chopped in the laboratory, 4560, 40,680, 108,000, and 896,154 germs per gramme, and retained their color four or five hours. When they became changed in color, the addition of 0.5 per cent. of sulphite restored the original appearance, but after forty-eight hours this could not be done.

A recent investigation of the action of sodium sulphite on dogs by Kionka[4] is confirmative of conclusions held generally, that sulphites are

[1] Archiv f. Hygiene, xl. p. 291.
[2] Chemiker-Zeitung, 1901, p. 794.
[3] Hygienische Rundschau, 1901, p. 877.
[4] Deutsche med. Wochenschrift, February 6, 1902.

a most undesirable admixture to foods. The dogs were fed for sixty days, or longer, with meat containing from 1 to 2 grammes per kilo, and when killed showed invariably extensive changes in the circulatory system, hemorrhages, inflammatory and degenerative processes in the lungs, kidneys, intestines, heart, and liver.

Formaldehyde. Contrary to general opinion concerning the undesirability of the presence of formaldehyde in milk, Tunnicliffe and Rosenheim,[1] experimenting with young children, concluded that milk containing 1 part in 5000 could be consumed with perfect safety, and that this agent, as commonly used, has no influence on the general condition; but, as is the case with so many disputed questions, other experimenters have come to directly opposite conclusions. It is, indeed, difficult to understand how a substance, which even in very dilute conditions can have such decided local action on the skin, can fail, even when much more dilute, to have some irritant action on the much more sensitive mucosa of the digestive tract.

Salicylic Acid. Many countries expressly prohibit the use of salicylic acid as a food preservative, since it is generally conceded that even small amounts thereof, taken continually into the system, exert a deleterious influence. Recent investigations, which show that this substance may be present normally in minute amounts in fruits and natural wines, are therefore interesting in that they suggest caution on the part of food analysts in reporting adulteration when none has been practised. Thus, Portes and Desmoulieres[2] found unmistakable traces in ten different kinds of strawberries, and Pellet[3] found about 0.8 milligramme per litre in certain natural wines. The methods employed in both series of experiments were such as to leave no doubt as to the correctness of the conclusion that the substance isolated was salicylic acid.

MEAT-INSPECTION.

Following are some of the provisions of the German meat-inspection law, which has excited so much interest in this country because of the announcement, in February, 1902, that it would go into full effect on October 1. Chapter A of the law prescribes in forty-eight sections the system of inspection and treatment of animals, slaughter-houses, and meats. This chapter is opposed bitterly by a large part of the population of Germany, other than the agricultural classes, and it is believed that it will increase the cost of the very inadequate supply of home-grown meat. Chapter B provides for the examination and qualification

[1] Journal of Hygiene, July, 1901, p. 321.
[2] Annal. chim. analyt., 1901, p. 401.
[3] Ibid., p. 327.

of inspectors, who are required to be competent veterinarians. Chapter C covers the code of instructions for sub-inspectors, who are not required to be educated as veterinarians. Chapter D prescribes the regulations for inspection and sanitary treatment of foreign meats presented for import. Chapter E deals with the whole subject of trichinæ and pork meats, both native and foreign grown.

Fresh meats may be imported only in whole carcasses. Carcasses of cattle and hogs may be split, but the halves must be left together and must be accompanied in every case by the head, lungs, heart, and kidneys. Calves may not be split. Cow beef must include the udder, and pig carcasses must include the tongue. With the exception of hams, bacon, and intestines, no piece of pickled, smoked, or otherwise preserved meat may be imported if it weighs less than 8.8 pounds avoirdupois.

Paragraph 21 prohibits the importation of meat preserved with borax or boric acid, or with any of a number of other antiseptics which, hitherto, have been used more or less extensively as preservative agents.

It is predicted that, with the enforcement of this very stringent law, the Germans will have a meat famine. Even in June, the importations from Denmark, Austria, and elsewhere were so small that the price of beef was practically prohibitive.

LEPROSY AND FISH.

Mr. Jonathan Hutchinson is still strenuous in asserting that leprosy is caused by eating raw or badly cured fish. He is not at all deterred by the fact that, in parts of India where neither fish nor meat is eaten, leprosy prevails extensively. He believes that the specific bacillus will soon be found in fish, and he has no patience with those who believe that the disease is contagious. In opposition to Hutchinson, Dr. A. S. Ashmead[1] quotes from a letter from Dr. Grenfell, the superintendent of a mission for deep-sea fishermen operating in Labrador, who says: "To the best of my knowledge, I have never seen a case, or anything resembling leprosy, among this population, who are so poor and who live on fish."

According to E. F. Neve,[2] it is possible that there are about 300 cases of leprosy in a population of about 1,000,000 in Kashmir. All but very few of the cases are among herdsmen in the mountains, or farmers who mingle freely with them. The cases are more common among men than among women; in fact, 90 per cent. of the victims are men. Neve made a thorough investigation of the food-supply with

[1] American Medicine, July 19, 1902. [2] British Medical Journal, May 3, 1901.

reference to fish, in an endeavor to determine the truth of Mr. Hutchinson's hypothesis so far as these cases are concerned, but found that it does not hold.

According to Dr. Hansen, of Bergen, the people of Norway are now eating more fish than ever before, but, nevertheless, leprosy is rapidly diminishing, owing to segregation.

INSECTS AND HUMAN DISEASE.

C. von Holub[1] makes the interesting communication that he has succeeded in infecting insects of different species with the streptobacillus of Ducrey, the cause of *ulcus molle*, in more than 1000 cases. After inoculation, each insect became, within several days, literally a package of pure culture of the organism. Every part of the organism —head, thorax, and abdomen—was filled with the bacteria, and, although in the beginning there was in the pus of the ulcer a mixture of bacilli and cocci, in the insects there was nothing but pure cultures of the streptobacillus. Among the inoculated insects, those which were fed lived not longer than twenty-one days, but those that were not fed lived only two weeks. Twelve hours after infection, the development of the micro-organism could already be observed.

The following proved to be susceptible to infection: orthoptera, rhynchota, hemiptera, coleoptera, lepidoptera, diptera, and hymenoptera. Inoculation was performed by means of a very slender and sharp sterilized needle. The infected males conveyed the disease to members of the other sex, and in cages where numbers of insects were kept with only one that was inoculated, all the rest became infected. Feeding with pus also caused infection.

MALARIA.

Since the general acceptance of the theory of transmission of malaria by mosquitoes, much has been done by individuals and governmental authorities in investigating ways and means for the prevention of mosquito-breeding, for the destruction of anopheles larvæ, and for the protection of the individual from infection. In many places, effort has been directed toward diminishing the opportunities for breeding by drainage of surface collections of water, and with marked success. Where removal of the breeding-places is not possible, the application of the cheapest grade of petroleum in amount sufficient to form a very thin film (about an ounce to fifteen square feet of surface), repeated at

[1] Centralblatt f. Bakteriologie, etc., xxx. p. 284.

intervals of about seventeen days, is found to yield good results, since the adult female is thereby prevented from depositing her eggs, and larvæ from eggs already deposited are quickly destroyed. If the conditions are such that kerosene treatment is not within the range of practical politics, the natural enemies of the larvæ may be introduced. Of these Howard mentions, as most efficacious, sunfish, top-minnows, and sticklebacks.

In order to prevent the sick from becoming a source of infection for others, their rooms should be screened so that mosquitoes shall not have access to them; and in order to protect the well from the specific mosquitoes, their rooms, too, should be similarly treated. Those whose work obliges them to be out-of-doors at night should wear gloves and also headpieces made with mosquito-netting. Local applications of essential oils are of but limited value.

Mosquitoes that have gained access to houses may be destroyed by fumigation with sulphur dioxide or by burning pyrethrum. The former was found by Rosenau[1] to be much more effective than formaldehyde gas against insect life. One pound of sulphur is recommended for each 1000 cubic feet of air space, or an equal weight of pyrethrum may be used.

The expedition to West Africa, under the direction of the Liverpool School of Tropical Medicine, has achieved excellent results. At Freetown, the most malarious areas have been thoroughly drained, and enormous improvement in the general health has been effected.

In the province of Basilicata, in the southern part of Italy, where malaria rages enormously, an aniline dye is used against the anopheles larvæ and is found to be efficient even in such weak dilution as 0.000031 per cent.

At the agricultural exposition at Palermo, in May, 1902, a department was devoted to exhibits bearing on the hygiene of malaria. This included a railway station, such as are now in use on Italian railways running through malarious districts, supplied with mosquito bars and containing dummies of operatives protected by mosquito veils, maps showing the districts in which the disease prevails extensively, and diagrams demonstrating the life history of the anopheles mosquito. The exhibit was designed to impress upon the public mind the great importance of prophylaxis.

Observation stations have been established in the most malarious parts of many provinces of Italy, and protective measures have been employed on many of the lines of railroad and elsewhere, the result being that in many of the protected zones malaria has diminished in a remarkable degree, while in unprotected regions it continues unabated.

[1] Bulletin No. 6, Hygiene Laboratory, U. S. M. H. S., September, 1901.

The government compels all laborers engaged in railway construction to remain indoors between sunset and sunrise (during which time the anopheles mosquitoes are most active), in houses with screened windows and doorways, and thus has reduced the prevalence of the disease among this class to a minimum.

Concerning the assertion that the malarial mosquito bites only between sunset and sunrise, Kohlbrügge[1] alleges that in the Malay Archipelago they bite at all times, although mostly in the evening, so that in that region it is most difficult to carry out preventive measures. But Plehn,[2] answering, says that he has been in all manner of tropical places, including Java, where, during a stay of several weeks, he observed that the danger of being stung by day is relatively small, excepting in dark rooms and in shady places in the woods. He asserts that, in order to avoid misconception, one should never speak of mosquitoes in general, but should state the genus concerned. According to Nuttall,[3] anopheles mosquitoes show a preference for certain colors, being attracted most by navy blue, then by dark red, reddish-brown, scarlet, black, and slate-gray. The colors which attract least are yellow, orange, white, and ochre. He quotes Joly as saying that, in Madagascar, mosquitoes are attracted more by brown than by red soil and white sand; that wearers of black stockings are bitten more than those who wear white, and that negroes are bitten more than whites. But Stevens and Christophers have shown that the mosquito is attracted by the odor of negroes, and this fact must be taken into account in this connection. Nuttall suggests the employment of traps (boxes lined with their favorite colors), in which the mosquitoes may be caught and destroyed. The attraction of dark colors has been noted also by Osborne Brown,[4] who advises, among other measures, the putting away of all dark clothes in which they may find refuge.

Although the anopheles mosquito is not a strong flier, it may be transported many miles, both by vehicles, such as railway cars, and by the wind. Dr. Kallock, of the United States Public Health and Marine Hospital Service, reported to the Supervising Surgeon-General, in August, 1901, that the captain of the ship *America* stated that mosquitoes (kind not specified) came aboard the vessel when she was at least ten miles from land. But under ordinary circumstances anopheles are not likely to move far from the place where they are bred.

That the presence of anopheles does not necessarily mean that malarial infection is to be expected, has been well shown by Nuttall and others. In England, Nuttall found anopheles larvæ in no less than 173 different

[1] Archiv f. Schiffs u. Tropenhygiene, v., p. 166.
[2] Ibid., p. 186.
[3] British Medical Journal, September 14, 1901, p. 668.
[4] Journal of Tropical Medicine, October 1, 1901.

localities, in some of which malaria, so far as known, has never existed. In France, Sergent[1] has found them in great abundance where malaria formerly was common, but now is and for twenty years has been unknown. In Germany, Pfeiffer[2] reports great numbers of them in districts formerly, but no longer, malarious; and in Italy, Celli[3] has found the insects in places where the disease never has existed.

In England, it appears that anopheles do not bite, although fairly common, but whether the same is true in the district described below is not stated; if they do, there must be some undiscovered local condition which prevents the disease. Celli and Gasperini[4] describe certain localities in Tuscany, which, less than thirty years ago, were very malarious, but to-day are quite free from malaria, although, so far as known, the same general condition obtains as formerly. The stagnant marsh water swarms with anopheles larvæ, and the air with myriads of the adult mosquitoes; there is no lack of the malarial parasite with which the mosquitoes might infect themselves, since the natives go to other parts of Italy and return with the disease; and yet, in spite of the presence of all of the recognized essential factors for an extensive epidemic, no outbreak occurs. The children are described as healthy and robust, and many adults who have never been out of the district have never had even the slightest attack of the fever. The population is by no means immune, for individuals are seized when they go to other districts in which the disease prevails, nor are the mosquitoes incapable of acquiring infective properties, for specimens carried to Rome for experimental purposes will readily bite persons having the disease. Freedom from infection is not to be attributed to the use of quinine, since that drug is not used any more extensively than elsewhere.

That malaria cannot prevail in the absence of anopheles, is illustrated by the fact that in Barbadoes, although filariasis, spread by *Culix fatigans* and other *Culices*, is common, malaria does not exist. Low[5] visited a swamp at Worthing, three miles south of Bridgetown, and made a careful but unsuccessful search for larvæ of anopheles. He visited other collections of water in other parts of the island, but his search was negative in results in each instance. Leaving Barbadoes for St. Vincent, he took with him a plentiful supply of water from the Worthing swamp, in order to determine whether there was anything in the water which might be prejudicial to life and growth of anopheles larvæ. It was found that the larvæ of *A. albipes*, the common West

[1] Annales de l'Institut Pasteur, October 25, 1901.
[2] Correspondenzblatt des allgemeinen ärztlichen Vereins von Thüringen, 1901, No. 7.
[3] Centralblatt f. Bakteriologie, etc., xxviii. p. 534.
[4] Ibid., October 23, 1901, p. 523.
[5] British Medical Journal, January 25, 1902.

Indian anopheles, taken from a swamp at Calbaqua, three miles from Kingstown, the chief town of the island, would live perfectly well in the water, and would develop and mature without difficulty. Low suggests the seriousness for Barbadoes of the possible introduction of anopheles mosquitoes into the Worthing swamp.

YELLOW FEVER.

On the etiology of yellow fever, Reed and Carroll[1] have made additional communications of great interest. They state that, although they have demonstrated that the specific agent of the disease is present in the blood, prolonged microscopic search by themselves and others, both with fresh and stained preparations of blood taken at various stages and during early convalescence, have proved entirely negative, as have also their investigations of the bodies of infected mosquitoes dissected in a fresh state and also after hardening.

Dr. Welch, of Johns Hopkins University, called their attention to the important observations of Loeffler and Frosch on the cause of foot-and-mouth disease. These investigators discovered that immunity could be conferred upon cattle by the subcutaneous or intravenous injection of $\frac{1}{40}$ to $\frac{1}{5}$ c.c. of pure lymph previously mixed with 1 c.c. of defibrinated blood of an animal that had recently recovered from the disease, and they then wished to ascertain whether calves could not be immunized by injection of this filtered lymph. They found that calves so treated developed the disease with the same promptness as calves that had been treated with the same amount of the lymph in an unfiltered condition. This indicated either that the filtered lymph contained an extraordinarily active toxin, or that the bacterium of the disease was so minute that it could pass through the filter, which holds back the smallest known bacteria. It appeared from subsequent investigation that the latter explanation was the more plausible.

For the purpose of determining whether observations conducted along the same lines might throw additional light upon the etiology of yellow fever, Reed and Carroll decided upon a series of experiments, which were begun in August, 1901. On the day of Dr. Carroll's arrival in Havana, the first patient of a series of 7 cases of yellow fever which Dr. Guitéras had produced by bites of infected mosquitoes was taken sick; but since, for several reasons, it was not practicable to withdraw blood from any case under treatment in the city of Havana, it became necessary to produce cases by means of bites of infected mosquitoes. Volunteers were obtained, and two acquired the disease. From one of

[1] American Medicine, February 22, 1902.

these blood was drawn on the second day, and ten drops thereof were immediately added to each of four flasks of sterile nutritive bouillon. These were kept under the usual conditions for two weeks, with no development of growth. From the second case, at the beginning of the third day, 65 c.c. of blood were taken from a vein at the bend of the elbow. This was placed in a sterile test-tube and set aside in a refrigerator. Five and a half hours later, 19 c.c. of the slightly blood-stained serum were drawn off into another tube. Then this was diluted with an equal quantity of sterilized distilled water, and the mixture was filtered through a new Berkefeld filter that had been sterilized in an Arnold sterilizer. In this way 35 c.c. were obtained. The 19 c.c. that had been drawn off were replaced with water, and the whole mixture—clot, serum, and distilled water—was poured into a sterile dish and whipped up with a sterilized egg-beater. The mixture was divided into two parts, one of which was reserved for inoculation of a control subject, and the other heated to 55° C. for ten minutes. Thus, three kinds of material were at hand from the blood of Case II., namely: (*a*) The unheated and partially defibrinated blood; (*b*) the partially defibrinated blood which had been heated to a temperature of 55° C. for ten minutes, and (*c*) the diluted serum which had been filtered through a Berkefeld filter. Each of these three materials was used for the inoculation of one or more individuals, with the following results:

Case III. Subcutaneous injection of 0.75 c.c. of *a*, fifteen and a half hours after the blood was drawn. The earliest symptom came on in five days and two hours. The case proved to be genuine yellow fever, and ran a mild course.

Cases IV., V., and VI. Three subjects received subcutaneous injections of 1.5 c.c. of *b*, but nothing resulted from them. Thus, it is proved that the specific agent present in the blood is destroyed by a temperature of 55° C. maintained for ten minutes.

Case VII. An American soldier, non-immune, received an injection of 3 c.c. of the serum filtrate, representing 1.5 c.c. of the undiluted serum. Symptoms appeared in four days and four hours, and on the fourth day of their course the man was visited by the Board of Experts, who confirmed the diagnosis of yellow fever. Recovery followed.

Case VIII. Another American soldier, non-immune, was similarly treated. The first symptoms appeared in four days and one hour, and a typical case of yellow fever developed. Diagnosis was confirmed by the Board of Experts. The patient made a good recovery.

Case IX. An American, non-immune, received subcutaneously the same amount of the diluted and filtered serum as was administered to the subjects of Cases VII. and VIII. After an interval of four days

and a half hour, he complained of headache and flashes of heat, with slight pain between the shoulders, and his temperature was elevated a fraction of a degree. In six hours his temperature had fallen, and on the following day the patient's condition was normal.

To summarize briefly, one subject treated with the unheated and partially defibrinated blood passed through a mild but typical attack of yellow fever, and recovered; two out of three who received subcutaneous injections of filtered blood serum developed unmistakable attacks of yellow fever after periods of incubation of 98.5 and 100 hours, respectively, while the third gave negative results; and three subjects who were treated with the partially defibrinated blood which had been heated to 55° C. for ten minutes yielded negative results.

In order that the Berkefeld filter which had been used in filtering the serum should be thoroughly tested, it was first resterilized by steam, and then a recent bouillon culture of staphylococcus pyogenes aureus was passed through. The filtrate proved to be sterile, and hence the filter was reliable for the delivery of a bacteria-free filtrate. As in the case of the serum of foot-and-mouth disease, the occurrence of the disease under the circumstances and within the usual period of incubation may be explained in one of two ways: the serum filtrate contains a powerful toxin, or the specific organism of the disease is of such minute size that it can pass readily through the pores of a Berkefeld filter. In favor of the toxin supposition they cite: "The early and well-marked jaundice, the free hemorrhage from the mucous membranes of the mouth and stomach, doubtless due to profound changes in capillary vessel walls, the rapid progress of the disease to a fatal termination, the advanced fatty degeneration of the hepatic cells, as well as the marked parenchymatous changes found in the kidneys. If present in the blood, this toxin would, in all likelihood, be found in the serum filtrate obtained from the blood, and if injected in sufficient quantity might induce an attack of yellow fever in a susceptible individual after the usual period of incubation."

Against the toxin hypothesis, the authors draw attention to the innocuousness of the partially defibrinated blood when heated to 55° C. for ten minutes, as shown by the negative results of Cases IV., V., and VI., for, although certain bacteria are destroyed by that temperature, no toxin is known as yet that is destroyed by so low a temperature maintained for so short a time. Thus, destruction of the tetanus toxin, which is the most sensitive known, requires twenty minutes' exposure to 60° C., or 1.5 hours' exposure to 55° C.

"As a further test, and in order to determine whether the filtered serum contained something more particulate than a soluble toxin," the authors injected into one of the subjects who had yielded negative results,

but who desired to have his immunity tested farther, 1.5 c.c. of blood drawn from the venous circulation of Case VII. early in the fourth day of the disease. It was held that, if it was found that the injection of so small a quantity of blood was followed by an attack in a third individual, the evidence would point in the strongest manner to the presence of the specific agent of the disease in such blood, since it would be hardly probable that a toxin so greatly diluted in the body of the second individual would still be capable of producing the disease. The subject of the experiment showed premonitory symptoms after an incubation period of exactly twenty-four hours, and developed a typical, though mild, case of yellow fever, the diagnosis of which was confirmed by the Board of Experts. The authors conclude that the blood of Case VII. contained the specific agent, which is so small that it will pass a Berkefeld filter.

Concerning the supposed agency of fomites in spreading yellow fever, the experiments of Reed, Carroll, and Agramonte[1] are of great value and interest. Three large boxes of sheets, blankets, pillow-cases, etc., contaminated with black vomit, urine, and feces of yellow fever patients, many of them purposely smeared therewith, were placed in a building of 2800 cubic feet capacity, tightly ceiled and battened, with small windows to prevent thorough circulation of air, and wooden shutters to prevent the disinfectant action of sunlight. The windows were covered with wire gauze, and the entrance with a screen door. The boxes were unpacked by three volunteer subjects, and their contents were shaken so that the specific agent, if present, might be disseminated throughout the air of the room. The different articles were then used on the three beds provided, and some were hung about the room and near the beds. For twenty consecutive nights the three beds were occupied by the volunteers, who every morning packed the filthy articles back into the boxes, and every evening unpacked and distributed them again. During their tour of service, other bedding, soiled with the bloody stools of a fatal case, was received in a most offensive, stinking condition, and used like the rest. Then other non-immunes repeated the experiment for twenty-one nights, and these were followed by others who, for fourteen nights out of twenty, slept with pillows covered with towels that had been thoroughly soiled with blood drawn from a case of well-marked yellow fever on the first day of the disease. The result of the exposure of these seven non-immunes in relays for nine weeks was wholly negative. In the case of a man who was exposed in a building of similar size, thoroughly ventilated, containing only disinfected articles plus infected mosquitoes, the result was differ-

[1] Medical Record, October 26, 1901.

ent. Fifteen of the insects were set free, and he was soon bitten several times; later he was bitten again, and also on the following day. He developed unmistakable yellow fever, but two men who for eighteen nights occupied a half of the room, screened from the first by netting, escaped without a symptom.

A series of similar experiments by Dr. J. W. Ross, U. S. N.,[1] Director of Las Animas Hospital, gave confirmatory results. In the city of Havana, rooms were selected in buildings constructed of masonry, like those occupied by the poorer classes—damp, poorly lighted, and badly ventilated. The rooms were thoroughly renovated, and were made mosquito-proof by wire gauze; all cracks and rough places were sealed smoothly, and an abundance of pyrethrum powder was burned in the rooms so as to preclude the possibility of the presence of any mosquitoes. One room was fitted with furniture, etc., that had been disinfected with thoroughness, and in the other were placed bundles of bedclothes, bedding, and clothing that had been used recently by patients ill with yellow fever, many of them badly soiled with discharges and excreta. Eight non-immunes, in pairs, were kept, consecutively, a week in the normal clean room, and then transferred to the experimental room for a similar period. The results were wholly negative.

Preventive measures against yellow fever are in most respects the same as recommended against malaria. In addition to screening the sick so that they may not transmit the infection to mosquitoes, which, in turn, may convey it to the well, it is necessary to screen also the dead, for stegomyia will bite both the living and the dead. The prevention of breeding and the destruction of larvæ require different methods of procedure than in the same work against anopheles, since they propagate in cisterns, and in all small collections of water in and about dwellings. Reed and Carroll found larvæ, for example, in cesspools, rainwater barrels, horse-troughs, sagging gutters, tin cans, etc. In New Orleans the Mosquito Commission found them in the majority of cisterns examined. According to Reed and Carroll, the eggs begin to hatch as a rule on the third day, the larval stage lasts seven or eight days, and the pupal stage two days. Thus, the period necessary for full development is much shorter than that required for any species of the malarial mosquito, and necessitates more frequent, and even constant, attention. Temperatures lower than 75° F. retard the process, and eggs kept at 68° F. do not hatch, although larvæ kept at that temperature develop, although very slowly; kept at 50° F., larvæ fail to reach maturity. The eggs are very resistant to low temperatures and to dryness. Reed and Carroll observed that eggs dried on filter paper and

[1] New Orleans Medical and Surgical Journal, May, 1902, p. 711.

kept ninety days hatch quickly when placed in water, and that after being frozen for an hour and thawing at room temperature, they hatch on the sixth day in an incubator kept at 95° F.

The precautions with regard to out-door exposure between sunset and sunrise do not apply in the prophylaxis against yellow fever, for stegomyia are active much earlier than sunset. Although Reed and Carroll found them especially active in Cuba from 4 P.M. until midnight, the New Orleans Mosquito Commission[1] asserts that they are active during the day, and especially in the afternoon. Reed and Carroll state that, in captivity, the hungry impregnated female will bite at any hour. At temperatures below 62° F. they do not bite at all, which accounts for the decline of epidemics with the advent of late autumn.

When cases of yellow fever occur, it is advised that, since the specific mosquitoes breed in or near houses and do not fly far from their birthplaces, measures be taken to destroy, by means of sulphur dioxide or burning pyrethrum powder, all those in the houses concerned and in the neighboring houses as well. Non-immunes entering infected houses are advised to apply spirits of camphor, oil of pennyroyal, or 5 per cent. menthol ointment to all exposed surfaces and to the ankles as well, these agents exerting a temporary protection against being bitten.

For the prevention of epidemics of yellow fever, the importance of excluding infected mosquitoes must be borne in mind. It has been demonstrated that mosquitoes may be transported through long distances in railway cars and aboard vessels, and this fact led S. B. Grubbs[2] to conduct experiments to determine how long they may live when packed within trunks and other ordinary baggage and under different conditions of temperature and moisture. The results showed that it is possible for them to live in ordinary baggage several days, particularly if moisture be supplied.

The results of systematic effort in the destruction of larvæ and breeding places are demonstrated most clearly by conditions now prevailing in Havana. Under the direction of Dr. W. C. Gorgas, U. S. A.,[3] the "Stegomyia Brigade" began its work in March, 1901, when 16,000 houses were examined, and larvæ were found in more than that number of breeding places. The work was kept up continuously, and during December, when 16,121 houses were examined, less than 250 collections of larvæ were found. All collections of water were required by ordinance to be kept mosquito-proof, and violations of the ordinance were punished by fines. Every house was inspected, and all drains and cess-

[1] New Orleans Medical and Surgical Journal, January, 1902.
[2] Yellow Fever Institute Bulletin, March, 1902, No. 6.
[3] Public Health Reports, February 14, 1902, and Medical Record, July 19, 1902.

pools not otherwise protected were treated with kerosene. From May 7th to July 1st, there was no yellow fever in the city; then it was imported, but the number of cases during July and August reached only 12. During the entire year there were but 18 deaths from yellow fever, and 12 of these occurred before Gorgas began his work. During the previous forty-five years, the average number of deaths therefrom was 751.44, the minimum, 51, occurring in 1866. From September, 1901, to the time of writing (August, 1902), not a single case of the disease occurred in Havana.

TYPHOID FEVER.

Certain statements concerning the propagation of typhoid fever have been promulgated by Dr. M. A. Veeder,[1] and have attracted considerable attention, especially in the secular press. His idea is that the surest method of perpetuating the disease is by burying typhoid material in the soil, without first subjecting it to efficient disinfection. He asserts that B. typhosus grows to the surface like fungi in a hotbed; that it may contaminate the water supply; and that, having grown to the surface, the infection may be carried by flies or by the wind. Furthermore, he alleges that garden truck may be rendered dangerous through being contaminated. He suggests also the possibility of a spore stage during which the disease may be air-borne.

There is really nothing new in the most important part of the above, and were it not for the fact that it has reached the press, and that the public may be misled as to the relative importance of soil and water in the causation of the disease, it would need no extended notice. It is well known that the typhoid fever organism can retain its vitality under favoring conditions of warmth and moisture for a long time when buried in the soil. More than four years ago Robertson reported in the *British Medical Journal* (January 8, 1898) the results of some experiments conducted by him during the preceding years. He buried diluted cultures of the organism, one just beneath the sod, one at a depth of nine inches, and one at a depth of eighteen inches. After one hundred and thirty days the organisms in the uppermost layer were found to be active, and those which had been buried eighteen inches beneath the surface were found to have proliferated to such an extent that they had reached the surface layers. Later in the winter he obtained no growth; but in the spring he moistened the patches with very dilute sterile bouillon and succeeded in obtaining growths. Others have found that the organism will live for many months if it is not completely

[1] Medical Record, July 26, 1902.

dried, and that in an ordinary air-dried condition it lives without impairment of vitality for a number of days, and in that state may be blown about in dust.

Whether or not typhoid organisms can live in a given soil, depends very largely upon the character of that soil, as has been shown by the Local Government Board in England. It has been shown that virgin soils are destructive to the organism, irrespective of the amount of organic matter of vegetable origin which may be present. Added to polluted soil which has been sterilized, the organism has been found active after fifteen months.

Concerning the possibility that typhoid fever may be air-borne, may be cited the epidemic which occurred in a camp, formed at Diyatalawa, on high ground in Ceylon, for Boer prisoners of war. Quill[1] reports that 600 cases of the disease occurred, the infection having undoubtedly been imported from South Africa. The guard remained healthy for more than two months after the development of the epidemic. The water supply was examined chemically every week, and bacteriologically with frequency, and no fresh milk was allowed in camp. All carbonated water used in camp was from the same source as that used at a neighboring sanatorium, in which no typhoid fever occurred. No uncooked food of any description was used, and no peddlers of any kind were permitted to enter the grounds. All persons leaving the camp for whatever purpose were required to carry with them a supply of filtered water. On account of these sanitary regulations, which appear to have been thoroughly enforced, Quill believes that the infection was air-borne from an adjoining camp of prisoners, among whom there was an epidemic of typhoid fever, though the possibility of transmission through the agency of flies or specifically infected latrines must be borne in mind.

Leake[2] is of the opinion that dry earth latrines are responsible for nearly all the cases of typhoid fever that occurred in the garrison at Bermuda.

Vaughn[3] also believes that dissemination of the typhoid fever bacillus in dust through the air has been clearly demonstrated, but he believes that the most important means of dissemination of the disease is specifically polluted drinking-water. Frequently the infective agent is carried on the hands and clothing of nurses and other attendants. It is his belief that the disease is never spread by exhaled air, although the organism may exist in the sputum. The organism has been found

[1] Air-borne Typhoid. British Medical Journal, February 15, 1902.
[2] The Prevention of Enteric Fever in Armies. Ibid.
[3] Journal of the American Medical Association, April 19, 1902.

by L. Jehle[1] in pure culture in the sputum of a patient in the third week of the disease, in five separate examinations, and in 5 of 22 other cases. The organism has been found also by Jehle and others in the sputum of cases of bronchitis in which there were no lesions of the intestines, which indicates that the air-borne theory is by no means unreasonable.

In the opinion of Turner,[2] it is a mistake to attach very great importance to wind and flies in the causation of epidemics of typhoid fever. His experience of six years in South Africa has led him to believe that, in the great majority of cases, the cause is to be found in a polluted water supply. He does not deny the possibility of air-borne typhoid, but points out that, if dust infection were a predominating or even an important cause of typhoid fever, one would expect to find the disease most prevalent from shortly after the beginning of the dusty season until shortly after its close; but he notes, as a matter of fact, that it is during this very period that typhoid fever is least prevalent. On the other hand, it is during the wet season when, on account of heavy rain, there is no dust that the disease is most prevalent. Although conceding the possibility of the transmission of typhoid fever by flies, he points out that in South Africa flies begin to be troublesome long before typhoid fever prevails, and continue to be so long after its subsidence. In answer to the criticism that typhoid fever prevailed among the troops in spite of the fact that filters were provided, he asserts of his own knowledge that the filters were not generally used, and that where the commanding officer of a regiment enforced the use of filters the number of cases in that particular body was insignificant.

Schüder[3] has collected reports of 650 epidemics of typhoid fever in all parts of the world, 377 of which occurred in Germany, 140 in England, and 66 in France. It appears that 70.8 per cent. of these were due to contaminated water, 17 per cent. to contaminated milk, and 3.5 per cent. to other foods. In reality water as a cause preponderated even more than is here shown, because even among those attributed to milk and other foods, as oysters, etc., it is probable that with some of them a polluted water may have been a contributing if not the main cause.

Speaking also of the transmission of the disease from person to person, he takes as a measure of the danger the relation between the whole number of cases in certain hospitals and clinics and the number of cases occurring among the nursing staff and among other patients. Of 35,647 cases of the disease, 1179, that is to say, 3.3 per cent.,

[1] Wiener klin. Wochenschrift, February 27, 1902.
[2] Typhoid Fever in South Africa. British Medical Journal, February 15, 1902.
[3] Zeitschrift f. Hygiene u. Infectionskrankheiten, xxxviii. p. 343.

occurred among the nursing staff and other patients; of 23,554 cases in the Prussian military hospitals during the period 1881 to 1897, 1012, or 4.3 per cent., were among the personnel of the hospital, and 478, that is to say, 2 per cent., among patients who were present on account of other sickness. The vehicle of infection is chiefly the discharges and particularly the urine of those sick and convalescent. He recommends the protection of the nursing body by anti-typhoid inoculations according to the method of Marsden and Wright.

DENGUE.

An interesting paper on the propagation of this disease of hitherto unknown etiology has recently been contributed by Dr. Harris Graham,[1] Professor of Pathology in the American College, at Beyrout, Syria, in which he asserts that the disease is spread by infected mosquitoes in the same way that malaria and certain other diseases are disseminated. The genus responsible is Culex, a number of representatives of which were allowed to bite a patient suffering with the disease, and then were transported to a mountain village in which the disease was unknown, and allowed to bite two individuals apparently in good health. In both cases within six days typical attacks of dengue were produced. In the blood of every case examined, he found a parasite in some stage of development in the red corpuscle, and in some cases in the blood plasma also. The parasite possesses amœboid properties, and evidently belongs to the protozoa. Its life cycle is longer than that of the malarial parasite, and differs farther from the latter in that it forms no pigment during its growth. Flagellated forms also were seen, and flagellæ were observed in the plasma pushing their way among the corpuscles. "It may not be absolutely proved that this hæmatozoon is the cause of dengue, but its constant presence in the red corpuscles during the fever, its resemblance to the parasite of the Texas cattle fever, its likeness in manner of growth and mode of propagation (by the mosquito) to the malarial parasite, all point in the same direction, and lead us to believe by analogy, if by no other way, that in this parasite we have the cause of dengue."

SMALLPOX AND VACCINATION.

During the past year almost the entire country has been ravaged by smallpox to an extent unequalled within recent times, and the prevalence of the disease has served to draw attention once more to the

[1] Medical Record, February 8, 1902.

enormous benefit of Jenner's immortal discovery of the immunizing influence of vaccination. The anti-vaccinationist leagues, encouraged by a preceding period of non-prevalence of the disease, were everywhere active in assailing existing vaccination laws and moving for their modification or absolute repeal. The time was, however, ill chosen, for in the presence of a serious condition, individuals, communities, and public authorities could ill afford to listen to the arguments and pleadings of irrational bigots, and, instead, proceeded to protect themselves everywhere; and never before has the practice of vaccination been more widespread in this country. The anti-vaccinationist leaders were, however, more in earnest than ever, and in many places, notably in Massachusetts and Pennsylvania, demonstrated their sincerity by exposing themselves to infection, with results disastrous to themselves and to their families.

The anti-vaccinationist derived much comfort from the fact that a number of persons in Camden, N. J., and elsewhere, who had been vaccinated, were seized with tetanus, of which they died. Fifty-two of these cases have been analyzed by Dr. R. N. Willson,[1] who finds that in nearly if not quite all infection occurred where the virus was introduced. The exact time and method of infection cannot be proved absolutely and scientifically, but the grouping of a large number of cases in one locality, and following the employment of virus from a common source, would tend at first to indicate primary infection due to the same. On the other hand, however, the discordant chronic incubation period and acute symptoms, the almost uniformly fatal termination, the severity of the course of the infection, the millions of normal vaccinations with virus from the same source, the simultaneous deaths from tetanus known to be due to other causes, the diminution in the number of such infections that occurred following the greater exercise of care to secure asepsis throughout the period covered by the process of immunization, the fact that in every case in which particulars were obtained overabundant opportunity was offered for secondary infection by the tetanus organism, and, finally, the absolute failure of all bacteriological and inoculation experiments to indicate the presence of B. tetani or its toxin in the virus, indicate that the infection was secondary, and that it occurred, as a rule, about the time of the acme of the vaccinia. Of those who were treated with tetanus antitoxin, 13 in number, 10 (76.9 per cent.) died; of those not so treated but subjected to the customary routine treatment with chloral, bromides, opium, and more rarely physostigma, 7 recovered and 32 (82 per cent.) died. Attention is called to the fact that the tetanus organism is very

[1] Journal of the American Medical Association, May 10, 1902.

frequently present on the skin, and especially on that of persons who are uncleanly in their habits and exposed to the dust of street, garden, and stable. As is well known, the tetanus bacillus and its spores are very abundant in garden soil and road-dust, and appear to thrive especially well in horse manure.

Concerning the efficacy of recent vaccination, Dr. W. M. Welch[1] states that during the recent epidemic of smallpox in Philadelphia the admissions to the smallpox hospital comprised about an equal number of vaccinated and unvaccinated patients. The unvaccinated were mainly young children and adults in the prime of life, the proportion of children under ten years of age being quite large. The vaccinated patients were almost wholly adults who had been vaccinated in infancy or early childhood. No vaccinated child under five years was among those admitted, and but few, if any, under ten, excepting those who were vaccinated after they had been exposed to infection. With two exceptions, one a boy of ten years, with a single variolous vesicle, the other a boy of twelve years, with about two dozen vesicles which dried up and disappeared quickly, no patient admitted had been successfully vaccinated within ten years. In order to provide sufficient accommodations, fifty or sixty men were employed in the erection of additional buildings, and as they were obliged to come into close proximity with the patients, they were requested to submit to vaccination. All did so excepting two, and these took the disease. Later on, it was found necessary to provide still additional room, and other workmen were engaged, two of whom neglected to get vaccinated and were seized with the disease.

With reference to the question whether smallpox is an air-borne disease, Dr. J. C. Thresh[2] reported that the majority of the cases of the disease in the Orsett Union were due to the presence of smallpox ships of the Metropolitan Asylum Board, anchored in the Thames opposite Purfleet. In a later communication[3] he asserts that the danger of infection through the air has been much underestimated, and that the Orsett epidemic was due largely to the proximity of the floating hospitals. Among the cases at Purfleet a large proportion could not be traced to contact with pre-existing cases. In the rest of the district all the usual factors making for epidemic prevalence of the disease were present, with an unusually large proportion of unvaccinated children below the age of ten years, but everything pointed to some central continuous focus of infection (the smallpox ships), from which, according to most careful inquiry, the continuous flow of infection could be explained only on the hypothesis that it was air-borne.

[1] American Medicine, July 12, 1902, p. 51.
[2] Lancet, February 22, 1902.
[3] Ibid., April 26, 1902.

DIPHTHERIA.

According to a new theory regarding diphtheria, advanced by Behring and referred to by Schanz,[1] the diphtheria bacillus is ubiquitous and may be found at all times on the mucous membranes of all persons; yet only those sicken who have not sufficient of the necessary antitoxin in their blood. Wassermann and others believe that the majority of persons are thus protected, but that the antitoxin is not present in the newborn. Neisser and Kalmert have found large amounts of antitoxin in the blood of persons who have never had diphtheria, but who have had sickness in which both toxic and non-toxic Löffler bacilli were present on the mucous membranes; and it has been demonstrated that their blood, through its richness in antitoxin, affords protection against diphtheria. Schanz himself has for eight years maintained the correctness of the theory that the genuine diphtheria bacillus, the pseudodiphtheria bacillus of Löffler and Hoffmann, the xerosis bacillus, and a saprophyte always present in the conjunctival sac are one and the same, differing only in virulence.

The value of antitoxin in treatment of diphtheria is once more set forth in voluminous statistics, this time from Berlin, in which city during 1901 the deaths from that disease numbered 469, whereas before the employment of the serum treatment the deaths therefrom ranged between 1300 and 2600 annually.

BERIBERI.

Recent investigations and observations concerning this disease of mysterious etiology are confirmative of the theory, promulgated a few years ago, that the cause resides in the food supply. Vorderman, of the Dutch Colonial Medical Service, observed that in prisons where the inmates were given white (decorticated) rice, about 28 prisoners in 1000 were seized with beriberi, while in those where red rice was served the seizures amounted to about 1 in 10,000.

Grimm noted, in 1898, that Europeans in Japan were immune so long as they adhered to European diet. The disease disappeared from the Japanese navy after the ration had been revised according to Western notions, and also from the Japanese penal institutions after extensive changes in the dietary and in the methods of preparing food. An epidemic which occurred at Diego-Suarez in 1900 was investigated by Dr. de Schuttelaer,[2] who was convinced of the alimentary origin of

[1] British Medical Journal, January 7, 1902.
[2] Archives de médecine militaire, 1901, p. 470.

the disease by the fact that complete elimination of rice from the diet ended the outbreak, excepting among certain Chinese laborers who continued its use. The rice in use was old, decorticated, and changed from the normal. In this epidemic there were 180 cases with 37 deaths.

Recently Dr. H. A. Littlefield, U. S. V., has reported to the War Department that in the military prison of Lingayen, Pangasinan, in which the sanitary conditions were excellent, there was much beriberi among the inmates; whereas, in the civil prison, a quarter of a mile distant, in which the sanitary conditions were much less satisfactory, there was complete absence of the disease. It happened that the only difference in the food was in the rice, the civil prison being supplied with native rice and the military prison with Chinese white (decorticated) rice. In February, 1902, the use of the latter was discontinued, and in place thereof the native rice was given. At once there was a great change. No new cases developed, and among those then sick there were no deaths. Prior to the change about a dozen cases developed every month, and the mortality rate had been nearly 50 per cent. (five per month).

Additional evidence that the disease is of alimentary origin is given by Dr. Arthur Stanley,[1] who shows that in Shanghai the Chinese prisoners under municipal police supervision are much more extensively attacked by beriberi than are the general public. The incidence in four widely separated prisons, completely isolated in every respect, was of approximately the same degree, but greatest where the length of incarceration was most prolonged—namely, at the jail. None of the European or Indian staff at these places were affected, although they resided in the same compound. This excludes soil and immediate surroundings as a cause. The fact that the disease occurs mainly among natives aggregated for periods longer than one month favors the idea of its propagation by contagion. Again, the operation of the infective agent, whether conveyed in food, or by parasites, or by contagion, would be favored by aggregation of potentially infective units. The food supply of three of the four prisons was from different sources, but the rice in use in all four was found to be of poor quality, weevilly and mouldy. A change was made in the rice at all the prisons; an excellent quality of Annam rice was procured at an increased price. From the beginning of August the new rice was given out every three days. Toward the end of September the number of cases diminished markedly, and in October they ceased. In spite of this fact, and because of a to-be-expected seasonal diminution, Stanley says: "The results of the

[1] Journal of Hygiene, July 1, 1902, p. 369

rice experiment were therefore probably negative," which finding would suggest that whoever chose that particular time for experimentation had not all of the qualifications of a true scientific investigator. Stanley, in spite of an evident disinclination to believe in the rice theory, mentions the following facts which certainly support it: In Japanese prisons beriberi has become a rarity since the daily allowance of rice was changed to a mixture of barley and rice in the proportion of 6 to 4; in 1899 the prisoners at Nugata were fed on Chinese rice, and from January to March 400 of their number (1000) had beriberi; those supplied with white (decorticated) rice were affected more extensively than those supplied with red rice; in Corea, where the Japanese and Coreans live side by side, the former eat rice and have the disease, and the latter live chiefly on peas, without rice, and escape; in the Straits Settlements the Tamils decorticate their rice after it is cooked, and have very few cases of beriberi, while the Chinese and Malays eat rice that has been husked a year longer, and suffer extensively.

From a series of sixteen conclusions with which Stanley's paper terminates, the following may be quoted as bearing on the theory of alimentary origin:

6. Inasmuch as, apart from rice, the food-supply of three out of four prisons was from different sources, and a change of rice for all the prisons to one of recognized good quality produced no well-marked effect on the prevalence of the disease in two months, food infection would appear not to be a factor in the cause.

7. Beriberi being a peripheral neuritis, which is a pathological condition usually associated with toxæmia, food would, in the absence of a primary lesion (as in diphtheria), seem specially indicated as a cause. For the same reason the cause would be met with in specifically contaminated food rather than in either qualitative or quantitative changes in diet.

8. The marked and apparently primary degenerative action of beriberi on heart muscle, like that produced by diphtheria, and to a less degree by influenza and alcohol and arsenic poisoning, all of which may also cause peripheral neuritis, and the remarkable clinical resemblance of beriberi to diphtheria in the frequency of death from sudden heart failure, would indicate a form of chronic poisoning.

9. The identity of the pathological changes in beriberi, diphtheria, and arsenic and alcohol poisoning, and the grouping of alcoholic poisoning with ergotism, pellegra, and lathyrism, which are caused by poisons produced by parasites in vegetable foods, suggest the possibility of the cause of beriberi being a toxin derived from an extraneous parasite of some article of food.

11. The oft-repeated statement that a beriberi patient recovers

quickly when removed to a fresh locality may not indicate that this disease is a place-infection, but rather that the source of the toxin may be removed by change of residence.

13. Something more is required for the prevention of beriberi than attention to the general rules of sanitation, such as ventilation, cleanliness, and diet. Moreover, isolation of cases as they arise, followed by disinfection, does not suffice to limit the disease.

14. The maximum incidence of beriberi in Shanghai being at the end of the tropical summer (the remainder of the year being quite temperate), the liability to recurrence yearly at this season in the same patient would be compatible with the elaboration of a toxin favored in its origin by the period of maximum atmospheric heat and moisture.

TUBERCULOSIS.

Human and Bovine Tuberculosis. Since the announcement by Koch, in June, 1901, of his discovery of the non-identity of the bacilli of human and of bovine tuberculosis, which discovery had been made and announced three years previously by Prof. Theobald Smith, of Boston, there has been much discussion of the danger of transmission of the disease through milk and meat from the bovine species to man, and Koch's sweeping statement of the lack thereof, which is equivalent to advocating a discontinuance of inspection of herds except from a purely economical standpoint, has been almost unanimously condemned as hasty, ill-advised, and wanting in judgment. It seems probable, however, that no harm has been done, but, on the contrary, a useful purpose has been served, since research work on the subject has been stimulated.

In England, Delépine,[1] who is opposed to Koch's views, undertook inoculation experiments to determine whether the disease can be transmitted from man to animals. He used the mixed sputum of six tuberculous patients, and experimented with four calves which were not previously tested with tuberculin, but which were apparently healthy. One was inoculated directly into the lung; the second, subcutaneously; the third, into the peritoneum; the fourth was fed two quarts of milk containing ten times as much of the sputum as was inoculated into the others. The calf that was inoculated in the lung with 5 c.c. died on the sixth day of generalized tuberculosis not due to the inoculation. The second calf, inoculated with the same amount of sputum subcutaneously, died on the sixth day with a conspicuous enlargement of a gland five inches from the point of inoculation. The third, which

[1] British Medical Journal, 1901, No. 2130, p. 1224.

received 5 c.c. in the body cavity, showed no definite reaction after twenty-six days, but reacted in sixty-eight days, and exhibited on post-mortem examination marked tuberculosis of the peritoneum. The fourth, fed with 50 c.c. of mixed sputum with its food, died twenty-six days afterward with tubercular lesions along the alimentary tract, but with no evidence of tuberculosis in any other organ.

There was no evidence of any tendency toward resolution in any of the tubercular lesions. They were all fresh and in a progressive condition, and the evidence was considered by the author conclusive that the disease in two of the four cases was communicated by feeding and by inoculation into the peritoneum.

In France, Thomassen,[1] who also is opposed to Koch, experimented on two calves and two two-year-old heifers with tubercle bacilli of human origin. The inoculations were made under the skin, in the peritoneal cavity, and in the trachea. Great care was exercised to be certain that the animals were not tuberculous before the experiments began. In only one case was a generalized form of tuberculosis developed. In one, other local lesions were produced. He concludes that it is difficult, but not impossible, to produce tuberculosis in cattle by means of pure cultures of the human bacillus, and that the transmission of the disease from cattle to man is easier than from man to cattle, on account of the greater virulence of tubercle bacilli of bovine origin.

Among German investigators, Hueppe[2] is very strongly opposed to Koch's views. He believes that the experiments on calves thus far reported are insufficient in number, and that due consideration should be given to the question of breed. He recalls a former view concerning immunity of pigs to anthrax, based on experiments conducted by Bollinger, Ritt, and himself, which was overturned by later investigations showing a difference in susceptibility according to breed. He recalls, moreover, a case of successful production by Bollinger of the disease in a calf by means of the sputum of tuberculous subjects, before the discovery by Koch of the specific bacillus.

Concerning differences between the bacilli of human and bovine tuberculosis, Hueppe contends that one should not go too far in drawing conclusions from a small number of negative results. The bacilli of mammalian and of avian tuberculosis show greater differences than are observed between those of human and bovine origin, and yet Fischel and himself succeeded in cultivating the two kinds, so that each took on the properties of the other to such an extent that the mammalian species was virulent to poultry, and *vice versa*. Similarly, it has been shown

[1] Rec. Med. Vet., Paris, 1901, No. 17, p. 529.
[2] Berliner klin. Wochenschrift, 1901, No. 34, p. 876.

that the bacilli derived from different species of mammals are endowed with varying degrees of infectivity to guinea-pigs, but produce the disease with equal facility if different amounts are employed; and yet the differences in amount are not greater than are observed between cultures from the same species of mammal, but of different origin.

Virchow,[1] also, is very strong in opposition to Koch, who, he thinks, has gone altogether too far. He recalls having seen, from time to time, at the Charité, cases of unusually advanced peritoneal tuberculosis, due probably to food.

Arloing,[2] in opposition to Koch, calls attention to the fact that Koch himself has caused tuberculosis, although only to a limited extent in a pig, by means of bacilli of human origin. Arloing has succeeded in producing general infection in goats and donkeys with bacilli from human sources, but he was unable to obtain more than a local infection when he inoculated beeves. Therefore, he agrees with many others that the bovine differs from the human bacillus only in virulence, and that this property can be modified in one way and another so that eventually the two species may be intercommunicable.

Concerning the danger of transmission of tuberculosis to man through the milk of tuberculous cows, Hueppe[3] believes that it has been very greatly underestimated by Koch. He asserts that in infection through milk the primary lesion is not necessarily confined to the alimentary tract, for it may come in the air passages from infection in the mouth. He admits that primary tuberculosis of the intestine is rare in adults, but contends that in the young it is much more common than Koch is willing to concede.

Ravenel,[4] too, has long held that tuberculosis due to feeding may appear elsewhere than in the alimentary tract, and reports the cases of two cows which developed extensive pulmonary lesions, with none elsewhere, after being fed with tuberculous material. A similar view is held, according to Salmon,[5] by Sims Woodhead, St. Clair Thomson, and Lord Lister, who have demonstrated that "infection through the medium of food may not necessarily be accompanied by disease of the intestines. The organs first attacked after feeding on tubercular material may be the mesenteric glands and liver, or even the bronchial and mediastinal glands and lungs."

The action of the gastric juice on the bacillus of tuberculosis has been newly investigated by Garrière,[6] who found that twelve hours' contact

[1] Berliner klin. Wochenschrift, 1901, No. 31, p. 813.
[2] Revue de la Tuberculose, 1901, part 3.
[3] Loc. cit.
[4] Philadelphia Medical Journal, August 14, 1901, p. 284.
[5] Bulletin 33, Bureau of Animal Industry, 1901.
[6] Compt.-rend. de la Société de Biologie, 1901, p. 1093.

has absolutely no influence on virulence, and that longer contact has but little effect in diminishing it.

Biedert[1] has long believed (he published the fact in 1883) that tuberculosis is but seldom or never conveyed through milk, and cites the fact that, although in the Bavarian highlands the cattle are largely tuberculous, and the population lives chiefly on milk and milk products, tuberculosis is comparatively rare in man.

That the human subject may be infected locally by the bovine tubercle bacillus has been shown repeatedly. In June, 1900, Ravenel reported three cases of local tuberculosis in man caused by accidental inoculation of the bovine bacillus during the post-mortem examination of tuberculous cows. To these he now adds a fourth,[2] in which the history leaves no doubt as to the origin of the infecting agent. The patient, while performing autopsies on two tuberculous cows, wounded himself in the wrist on the flexor surface. The wound was washed thoroughly, and with no other treatment it healed promptly. About four weeks later the scar became red, prominent, and sensitive. Soon a nodule, 15 mm. long by 8 mm. wide, appeared. This was excised, and with a portion thereof two guinea-pigs were inoculated subcutaneously, and both developed generalized tuberculosis. Another portion of the nodule was reserved for microscopic examination, which gave the following:

"Sections stained with hæmatoxylin and eosin show a round-cell infiltration with a large area of necrosis in the centre. Toward the borders of this area are seen numerous giant cells having the nuclei arranged in wreath-like form. The entire process is confined almost wholly to the reticular layer of the corium. In sections stained with carbol fuchsin an unusually large number of tubercle bacilli are seen, as many as eight being counted in a single field, which is a rare occurrence in tuberculosis of the skin."

That there is a difference in virulence between the bacillus of human and that of bovine tuberculosis is generally admitted, the greater virulence belonging to the latter. This has been shown by D. A. de Jong,[3] who succeeded in producing the disease in the goat, dog, monkey, sheep, and steer by inoculation with bacilli from both sources, but the lesions produced were much more serious and extensive following inoculation with the bovine variety.

Arloing,[4] too, asserts that the virulence of the two kinds varies according to conditions within the system of the different organisms,

[1] Berliner klin. Wochenschrift, November 25, 1901.
[2] University of Pennsylvania Medical Bulletin, February, 1902.
[3] La Semaine Médicale, December 15, 1901.
[4] La Presse Médicale, February 12, 1902.

and, it would appear, to unexplainable differences between different races of the human bacilli. Thus, some pure cultures are found to possess infective properties, and others to be harmless when inoculated into cattle, sheep, and goats. But this does not shed any light upon the question whether there is any considerable danger of transmission of the disease to man through milk of tuberculous cows, or through tuberculous meat. Nor do positive results of local inoculation, such as have been reported, for instance, by Ravenel, prove very much concerning the intercommunicability of human and bovine tuberculosis. But these instances demonstrate that the bovine bacillus may find suitable conditions for multiplication in human tissue, and the food experiments of Delépine and others demonstrate the possibility of the human bacillus finding like favorable conditions in the bovine body.

The assertion is often made that the cattle of the great Western ranges are practically free from tuberculosis, owing to the fact that they are not subjected to the evil influences of confinement in ill-ventilated buildings; but, according to Dr. E. V. Hutchinson,[1] this is not true of cattle of particular ranges, for in California, at some of the large abattoirs, fully 1 per cent. of the cattle are tuberculous, and in certain herds the percentage runs higher. Within two years he has seen herds from a section of Oregon which have had as many as 16 per cent. which were tuberculous.

Destruction of Tuberculous Sputum. Prof. Schrötter, of Vienna, expressed the opinion at the British Congress on Tuberculosis, that the best way of disposing of tuberculous sputum is to destroy it completely. The sputum should be collected in suitable receptacles and burned. According to Ottolenghi, corrosive sublimate, 5 : 1000, or 7.5 or 8 : 1000, with or without the addition of hydrochloric acid or common salt, will disinfect dry sputum with certainty when sprayed upon it, and so will a 10 per cent. lysol solution. Ten per cent. milk of lime is without effect. He found that formaldehyde in 10 per cent. strength and chloride of lime in the same strength in powder form have no effect. Chloride of lime in solution, however, seems to diminish the virulence. Lysol is as good as corrosive, but costs more. In a recent paper[2] concerning the problem of disinfecting rooms which have been occupied by tuberculous patients, he contradicts and criticises Steinitz's assertion that a solution of corrosive sublimate of the strength of 2 : 1000 is efficient for application to walls, floor, and furniture, and reaffirms his belief that nothing short of 5 : 1000 will produce sterility even after twenty-four hours' contact. While it is better in such an

[1] American Medicine, February 22, 1902, p. 305.
[2] Münchener med. Wochenschrift, December 17, 1901.

important matter as disinfection to err on the side of safety, if at all, it must be said that, in the experience of others, the weaker of the above solutions has proven effective, and that Ottolenghi's findings as to the efficiency of formaldehyde are at variance with those who have had large experience with this agent. The writer, for example, has found repeatedly that in the disinfection of sputum even a 1 per cent. solution is effective with two hours' contact. Furthermore, he has found that chloride of lime in solution, milk of lime, 5 per cent. carbolic acid, and 5 per cent. cresol solutions are effective, while corrosive sublimate in the proportions commonly recommended and used is very uncertain.

PRACTICAL THERAPEUTIC REFERENDUM.

By E. Q. THORNTON, M.D.

Acetozone (Benzoyl-acetyl-peroxide). One of the difficulties long encountered in the internal use of antiseptics is the fact that they are so powerfully toxic as to require small doses, and this interferes with their efficacy. The new antiseptic acetozone, which, by bacteriological tests, has been found to be as energetic a germicide as bichloride of mercury, is said to be entirely non-toxic, and may be employed internally, externally, and by hypodermic injection without untoward effects. Its degree of concentration appears to be a matter of concern only when it is employed as a local application to the conjunctival or urethral mucous membranes. In such cases there is slight smarting if solutions are too concentrated. Acetozone is a crystalline substance, soluble in about 10,000 parts of cold water or 1000 parts of warm water. In aqueous solution it undergoes hydrolysis and slowly decomposes, therefore, such solutions should not be kept for more than forty-eight hours. The fact that the substance undergoes this change does not militate against the use of such solutions, as hydrolysis is necessary to the development of its full germicidal activity. The crystals are soluble, 1 in 20 of oil, slightly soluble in alcohol, and fairly soluble in ether and chloroform, all of which solvents, however, bring about its gradual decomposition. In fluid neutral petrolatum it is soluble to the extent of 5 per cent. and does not decompose. The substance, being a powerful oxidizer, is reduced by all organic matter, and is explosive if suddenly heated in a tightly stoppered bottle, or if triturated, compressed, or pounded. The chemical is placed upon the market diluted by an equal weight of inert absorbent powders, in which form it is said to be permanent, and can be handled with perfect safety ; but must not be placed in proximity to steam pipes, radiators, etc. For making antiseptic solutions for ordinary use, about 20 grains of the powder may be added to the quart of water contained in a capacious bottle and well shaken. Such a liquid will have a cloudy appearance, due to the suspension of the inert absorbent powder and to benzoic acid formed by hydrolysis of acetozone. If a perfectly clear solution is desired, such as is necessary when it is to be used as a spray, for irrigations, or for hypodermic injections, it may be filtered or permitted to stand until precipitation occurs and the clear supernatant liquid decanted. For internal administration it may be given in aqueous solu-

tions or in capsules. If the latter method is adopted the powder should be first diluted with lycopodium, sugar of milk, magnesium carbonate, precipitated calcium phosphate, or some other inert powdered substance, before being enclosed in capsules. The dose usually employed is from 1 to 5 grains (0.06 to 0.03 grammes).

As a dusting powder it is best diluted with from 100 to 500 parts of powdered boric acid, talcum, or magnesium carbonate, all of which should have been previously rendered sterile. It may also be combined with powdered zinc oxide or starch. Hard or soft petrolatum is the most suitable base with which to combine it for ointments.

Aside from the use of this remedy as an antiseptic in general surgery, it has been highly praised by Murdoch Chisholm[1] in a case of *malignant œdema* of both hands, which he reports as having recovered without amputation, due to the constant application of acetozone solution. The solution was applied by wrapping the hands in gauze soaked in a saturated solution of acetozone, opening abscesses and sponging them with acetozone, combined with supportive treatment. He considered this remedy particularly applicable to cases of malignant œdema, as the bacillus is anaërobic, and acetozone, being a powerful hyperperoxide, was applied unsparingly, hoping enough oxygen would be absorbed through the incision and skin to destroy the bacilli. At one time during the treatment of this case the supply of acetozone became exhausted, and he resorted to the use of bichloride of mercury solution, but the hands and arms became so inflamed it was necessary to discontinue that solution and again resort to acetozone. If Dr. Chisholm's deductions as to the absorption of oxygen through the skin and incision in this case are well founded, the remedy should also be the best possible antiseptic in the treatment of wounds in *tetanus*.

There is considerable difference of opinion as to the seat of the primary focus of infection in *typhoid fever*, and also as to the power of any internal antiseptic to modify the course of this disease. Dr. Eugene Wasdin[2] is strongly of the opinion that the infection in a majority of the cases of typhoid fever is primarily pulmonic, the primary colony of organisms being located at some point along the respiratory tract, and that the infection of the blood and the intestinal tract are secondary to this. With these views in mind he believes that the treatment should be directed more energetically toward the destruction or attenuation of the germs in their primary pulmonic, secondary intestinal, and terminal colonies. These effects he believed could be secured by the use of a suitable germicide, but heretofore we

[1] Therapeutic Gazette, August 15, 1902.

[2] American Medicine, February 8, 1902, and Therapeutic Gazette, May 15, 1902.

possessed none that, if given in large enough quantities, was not injurious to the patient. Since learning of the active germicidal and non-toxic properties of acetozone, he has recently been able to put his theories into practice, and with happy results. The chemical has been employed by him as a spray, and internally to destroy the germ in its primary lung colony and secondary intestinal colony, and by hypodermoclysis to combat terminal expressions, with the result that "the disease has been limited almost entirely to the expression of intoxication from the primary focus, the intestinal symptoms remaining in abeyance, and the disease has been shorn of its most disagreeable features." In twenty-four cases reported there were no deaths, and the duration of the disease was shortened. The treatment pursued by Dr. Wasdin in these cases was as follows: The patients were well purged by administering grain doses of calomel combined with grain doses of aloin, and 2-grain doses of guaiacol carbonate. This was followed by the daily administration of from 1500 to 2000 c.c. of a twenty-four-hour-old solution of acetozone. The diet consisted of milk, to which acetozone solution was added. An attempt was made to reach the colonies in the lungs by forced inspiration of the atomized solution. The remedy was given in 5-grain doses twice daily, inclosed in capsules. To combat high temperature, cold sponging or tubbing was resorted to. Not only did the odor of the stools become less fetid, but bacteriological examinations showed that the number of bacteria was quickly and markedly reduced; "in fact, in one case the dejecta was found to be absolutely sterile during the second week of the fever." In addition to its germicidal properties, Wasdin states that he found acetozone to be a diuretic which assists in eliminating the toxins.

I. A. Abt and E. Lackner[1] praise the remedy, and give the histories of forty cases of typhoid fever in children, with but two deaths, treated with acetozone.

Alboferin. This new iron and albumin compound is a brownish, nearly odorless powder, with a faintly saline taste; it is freely soluble in water, producing a solution of neutral reaction, which does not coagulate upon heating, nor decompose when kept for some time. It contains 0.68 per cent. of iron, 0.324 per cent. of phosphoric acid, and 90.14 per cent. of albumin. It is said not to stain the teeth, nor induce constipation, and as it passes through the stomach unchanged, does not disorder gastric digestion. The clinical report of A. Fuchs[2] is very favorable to its use in both *primary* and *secondary anæmias.*

[1] Therapeutic Gazette, October 15, 1902.
[2] Wiener klin. Wochenschrift, February 27, 1902.

The remedy is non-toxic, and may be administered in doses of from one to five grains or more.

℞.—Alboferin . . . . . ʒij.
Pone in capsulas No. xxiv.
Sig.—One capsule after meals.

℞.—Alboferin . . . . . ʒij.
Elix. aromat. . . . . fʒiij.
M. Sig.—Teaspoonful after meals.

Ambrosia and Solidago. Although ambrosia artemesofolia (ragweed, Roman wormwood, or hogweed) and solidago odora (golden rod) have both been employed to a limited extent as diuretics and diaphoretics, neither has ever been considered an active remedy. Ideas based upon the principle that many cases of *hay fever* in this climate are due to the pollen of these plants led Dr. H. Holbrooke Curtis to employ the remedies internally to immunize persons against periodic attacks of the malady. Recently this method of treatment has been tested by Dr. E. Fletcher Ingals,[1] and with some apparent benefit; but his inability to secure an entirely satisfactory supply of the remedy prevented a thorough trial. He has made arrangements with Parke, Davis & Co. to have a supply of the plants collected (during their flowering season), and from them to manufacture a reliable fluid extract. With such preparations he hopes to again test the remedies and report thereon. In the cases treated the patients were directed to begin by taking six drops (2 minims) of the combined fluid extract before each meal, and increase the dose six drops at each succeeding meal until the quantity reached sixty drops (20 minims) at each dose. In a few cases this dose was exceeded. If no disagreeable effects arose or no symptoms of hay fever appeared the remedy was to be continued in the maximum doses for one or two weeks, and then discontinued; but if the stomach became disturbed the dose was to be diminished for a day or two. If after discontinuing the remedy symptoms of hay fever appeared, patients were directed to commence the treatment again. In addition to the fluid extracts to be taken internally, the following spray was given to be used in the nasal cavities:

℞.—Resorcin . . . . . gr. v.
Adrenals (vel adrenalin chloride, gr. ss) . . . . ʒij.
Boric acid . . . . . gr. xvi.
Camphor water (hot) . . . . . fʒiv.
Glycerin . . . . . fʒss.
Distilled water . . . . . q. s. ad. fʒij.
Macerate for four hours, then filter.
Use as a spray to nose and eye five or ten times a day when needed.

This was to be used half as often throughout the hay fever season, even when there was no irritation. For a time Ingals directed that a

[1] Journal of American Medical Association, June 28, 1902.

few drops of the fluid extract should be added to the spray, but this was found to be irritating, and was discontinued. Of the whole number—eighteen—who tried the remedy, twelve (67 per cent.) stated that they were relieved by the internal remedy. In several of these cases, as the symptoms subsided, the drops were discontinued, whereupon the symptoms reappeared, but speedily disappeared when the medicine was begun again. Sixty per cent. of the cases were subject to asthma during the attack, and half of these reported that this symptom was benefited or entirely relieved (as they believed) by the internal medicine. Seventeen per cent. were benefited, but it was a question whether the results should not have been attributed to change of climate. The same percentage of cases stated that they observed no relief from the use of the remedy.

Anesthesin. Para-amido-benzoic Acid Ester. This new anæsthetic, named anesthesin by its originator, E. Ritsert, of Frankfort-on-the-Main, is closely allied to orthoform. It forms a white, inodorous tasteless powder, melting at 89.5° C. It is only slightly soluble in cold water, but more so in hot water, and dissolves freely in alcohol, ether, lard, lanolin and other fatty ointment bases, and also in melted cacao butter. It has been examined by Burg, Kobert and others, who found it to be non-toxic and free from any after-irritating effects. While it is probably less powerful than cocaine, it possesses the advantage over this substance of being safe for internal administration, or hypodermic use in comparatively large doses. Owing to the insolubility in water of anesthesin, its hydrochlorate, which is quite soluble, is most suitable for hypodermic injections. Carl von Noorden[1] highly recommends this new anæsthetic for internal administration (in doses of about 7½ grains, two or three times a day) in *gastric hyperæsthesia:* in the form of lozenges to relieve cough and dysphagia; in the form of suppositories to mitigate the pains of *hemorrhoids*, and in soluble bougies to relieve *vesical tenesmus*. Ointments containing about 10 per cent. of the anæsthetic have been found valuable for relieving *pruritus*, especially pruritus vulvæ of diabetes. The following are suggested formulæ:

For Gastric Hyperæsthesia.

℞.—Anesthesin . . . . . ℥ss.
Ft. chartulæ No. vi.
Sig.—One powder three times a day.

For Dysphagia.

℞.—Anesthesin . . . . . gr. xxiv.
Pulv. acaciæ . . . . . gr. xxiv.
Pulv. sacchari . . . . . ℥ij.
Aquæ rosæ . . . . . q. s.
Misce et ft. trochisi No. xii.
Sig.—Dissolve one lozenge in the mouth every three or four hours for painful hemorrhoids or fissure of the anus.

[1] Berliner klin. Wochenschrift, April 28, 1902.

℞.—Anesthesin . . . . . ℥ss.
Olei theobromatis . . . . . ℥j.
Misce et ft. suppositoria No. vi.
Sig.—Use suppository by the bowel ten minutes before defecating.

Ardor Urini or Vesical Tenesmus.

℞.—Anesthesin . . . . . ℥ss.
Olei theobromatis . . . . . f℥j.
Misce et ft. bougie No. vi.
Sig.—Use a bougie once or twice a day.

For Pruritus.

℞.—Anesthesin . . . . . gr. xxiv.
Adeps lanæ hydrosi . . . . . q. s. ad. f℥ss.
Misce et ft. unguentum.
Sig.—Apply freely.

Sengemann[1] reports that the use of anesthesin at von Mikulicz's clinic has been remarkably successful in relieving the pain of ulcerating carcinomata and as an anæsthetic prior to cauterization of granulating surfaces, with nitrate of silver.

While convinced that cocaine still remains the best local anæsthetic for minor operations, G. Spiess[2] considers orthoform and anesthesin of great value in treating painful cutaneous and other affections involving the nerve terminals. It is his opinion that the healing process is promoted, and really only begins when the reflex irritation of the vasomotor nerve terminals is abolished. Anesthesin prevents vasomotor irritation, and consequent hyperæmia and swelling, as the inflamed nerve terminals are soothed and the reflex communication interrupted.

Dunbar[3] enthusiastically recommends anesthesin hydrochlorate as an anæsthetic for the performance of minor surgical operations. He considers it not only a substitute for cocaine, but superior to it. His reasons for this belief are that when injected subcutaneously it is nontoxic, and its anæsthetic effects persist at its height for more than thirty minutes. Furthermore, aqueous solutions of it are stable, and may be sterilized by boiling without deterioration. The formula suggested by him for subcutaneous injections is as follows:

℞.—Anesthesin hydrochloratis	gr. iv.	0.25	gm.
Sodii chloridi	gr. ij.	0.15	gm.
Morphinæ hydrochloratis	gr. ¼	0.015	gm.
Aquæ dest. . . . . q. s. ad.	f℥iij.	100.00	c.c.

Apocynum Cannabinum. The infusion and other preparations of apocynum cannabinum were used considerably at one time in treating renal and cardiac dropsy, but at the present date the drug is scarcely known to the younger physicians. It is stated on good authority that

[1] Centralblatt f. Chir., May 31, 1902.
[2] Münchener med. Wochenschrift, September 30, 1902.
[3] Deutsche med. Wochenschrift, May 29, 1902.

it became a common practice among some manufacturing drug houses to substitute apocynum androsæmifolium for the first-named drug, and this being almost devoid of any of the properties of apocynum cannabinum, physicians failing to secure beneficial effects by its administration naturally discontinued its use. During the past few years, manufacturers are taking particular pains in selecting apocynum cannabinum for making the tincture and fluid extract, and the remedy seems to be again coming into favor with a number of physicians. It is being employed in the treatment of *cardiac* and *renal dropsy*. The physiological action of the drug would seem to indicate that it is best suited to the same class of cases for which digitalis is found useful, as it is a stimulant to the heart, and raises arterial tension. When given in overdoses it is a gastro-intestinal irritant and induces vomiting and purging, accompanied by rather profuse sweating. Galubinine[1] states that when full doses are required gastro-intestinal irritation may be prevented by combining it with moderate doses of cannabis indica. M. S. Hildreth[2] obtained most satisfactory results from apocynum cannabinum in treating cases of cardiac dropsy and general anasarca following pregnancy, and considers it a remedy of exceptional value for relieving the œdema accompanying varicose conditions and varicose ulcers in elderly persons. The usual dose of the *tincture* of apocynum is from 5 to 20 minims; of the *fluid extract*, 1 to 5 minims three or four times a day.

Apomorphine Hydrochlorate. The value of apomorphine hydrochlorate as a *nervous sedative* was recognized by Wallender nearly forty years ago, and since that time the remedy has been used by a limited number of physicians to induce sleep, abort epileptic crisis, to quiet maniacal raving, and relieve violent choreic movements. The hypnotic and sedative properties of the drug seem to have been overlooked by many until Charles J. Douglas, in his publications, called attention to its value when used hypodermically in small doses for relieving nervousness and inducing sleep in the different stages of *alcoholism*. That the drug is a valuable hypnotic for hard drinkers who have taken more than their usual quantity, and for chronic alcoholics who have abstained from food for several days while continuing to drink, and are in a highly nervous state, is testified to by Warren Coleman and Polk.[3] They found the remedy valueless in delirium tremens, and by reason of its depressing action in such cases its administration may even be attended with danger. They administered apomorphine hydrochlorate hypodermically in twenty-eight cases classified by them

[1] Journal des Praticiens, August 17, 1901.
[2] Medical News, October 11, 1902.
[3] American Medicine, March 8, 1902.

as hard drinkers who had taken more than their usual quantity, twenty-two of which slept as a result of this drug; furthermore, sleep was induced in fifteen out of twenty chronic alcoholics who were very nervous and shaky. The effect of the drug, while mildly sedative, was unsatisfactory as a hypnotic when given to twenty chronic alcoholic patients bordering upon or actually in delirium tremens. In a number of instances when given by the mouth the remedy exerted a mild sedative effect, but did not induce sleep. Alcoholics who did well under apomorphine injections slept for several hours, and this treatment was followed in two or three hours by some recognized hypnotic, such as the bromides, chloral, or paraldehyde. When used with discrimination there is no doubt that apomorphine is one of many remedies that can be used with good effect in the class of cases under discussion, but if administered too freely it may give rise to immediate untoward effects, or be followed by a long period of physical depression. Dr. Perry[1] states it as his opinion that apomorphine is one of the principal remedies employed in many of the irregular institutions for the cure of alcoholism, and that the indiscriminate and improper use of the drug in these so-called "cures" not infrequently leads to suffering and depression, from which the subject is a long time recovering. The use of apomorphine for arresting attacks of *hysteria*, *hystero-epilepsy*, or even epilepsy is recommended by E. V. Foucher.[2] He suggests that $\frac{1}{10}$ to $\frac{1}{15}$ grain of apomorphine should be injected subcutaneously just before the onset or during the fit. The attention of hysterical patients is diverted by the injection, the vomiting, and subsequent depression, while at the same time nervousness is controlled. In epileptics, aside from the sedative influence of the drug, he believes its good effect is in no small measure due to the vomiting which unloads the overdistended stomach, as it has been observed by him that attacks often follow a heavy meal. We can hardly conceive it a safe procedure to induce vomiting in patients who are unconscious and breathing stertorously. It is needless to call attention to the dangers of such a procedure, especially if the patient has partaken of food a short time before.

Dr. T. Neal Kitchens[3] used apomorphine hydrochlorate hypodermically in doses of $\frac{1}{20}$ grain as an antispasmodic and diaphoretic in treating *eclampsia*, and was satisfied that it was of value.

Aspirin. By reason of the irritating and nauseating properties of salicylic acid and the alkaline salicylates, we are frequently driven to

[1] Boston Medical and Surgical Journal, August 22, 1902.
[2] Bull. Med. de Quebec, January, 1902.
[3] Therapeutic Gazette, August 15, 1902.

the use of the somewhat less powerful but more agreeable synthetics, salol, salophen, or aspirin. The actions of all of these last-named substances, while closely related, are not entirely similar. All are antirheumatics, and salol is also an intestinal antiseptic. Salophen has the same properties as salol, but is less toxic. Aspirin is said to be less toxic than either of these, and in addition to its antirheumatic property is a decided antipyretic.

Heinrich Singer[1] studied the action of the drug upon intestinal fermentation, and found it to be without effect, and denies the statements that aspirin is an intestinal antiseptic. J. A. Hale[2] considers aspirin less toxic and irritating than salicylic acid or the alkaline salicylates, and more satisfactory than either of these or salophen in treating the rheumatic pains of children. In the hands of S. Merkel,[3] aspirin acted very favorably in *joint rheumatism, gout, dry and exudative pleurisy,* as well as in *muscular rheumatism.* He observed the same pain-relieving action after aspirin as with sodium salicylate. In his cases there was an absence of untoward effects such as nausea, vomiting, roaring in the ears, headache, vertigo, and anorexia, except in one case, that of a woman who took 5 grains of aspirin during the day, and complained of roaring in the ears. Wohlgemuth accounts for the lack of these ill-effects by the fact that aspirin passes the stomach unchanged, and is only split into its components by the alkaline juices of the small intestines. According to Merkel this remedy can be given to patients with delicate stomachs, and he reports the case of a woman who took 10 grammes of aspirin in four days without showing any ill-effects. Merkel further reports the very favorable results obtained by him in four severe cases of podagra. He found it of little value in chronic gout.

Bromocoll. Numerous attempts have been made during the past few years to secure the combination of bromine with inert organic substances, as it is believed that many of the disagreeable features of inorganic bromides are due, to a certain extent, to the basic radical of the salts. This is undoubtedly so in the case of the most generally used salt—potassium bromide—which, in large doses, is distinctly depressant to the circulation and respiration. I have previously discussed in these pages *bromopin* (which is made by treating oil of sesame with bromine) and *bromalin,* a combination of bromine with formalin.

Bromocoll, the most recent organic bromine compound, is a tasteless powder, made by chemically uniting bromine, tannin, and gelatin. It is said to contain about 20 per cent. of bromine, is an energetic, nervous

[1] Zeitschrift f. klin. Medicin, Band xliv., Heft 1 and 2.
[2] Pediatrics, July 15, 1901. [3] Münchener med. Wochenschrift, April 2, 1902.

sedative, easy of administration, less expensive than potassium bromide, and about as powerful. The remedy has been used with good effect by Reich and Ehrke[1] in treating *epileptics*. They found that, in addition to its being a pleasant means of administering bromine, acne only rarely followed its use, even after large doses to especially predisposed subjects. They believe the remedy should be tried when other bromides are not well borne, and that its freedom from disagreeable features and its relative cheapness are deserving of recognition. It may be prescribed in powders, cachets, or capsules.

℞.—Bromocoll . . . . . ʒij.
Ft. chart. No. xii.
Sig.—One to three powders three times a day.

Atropine. It is our opinion that the value of atropine in some cases of *intestinal obstruction* has been established. Under its influence evacuation of the bowels is frequently secured; nausea, vomiting, and pain are relieved, and the circulation is supported. Fully considering the possible value of the drug for overcoming obstruction in some cases, I believe it to be a serious error to consider it a substitute for operative procedures. In *ileus* it should only be employed when operation must be delayed or is refused, or when by reason of the poor physical condition of the patient, as, for instance, in diabetes, extensive surgical interference is contraindicated. When atropine is given to overcome intestinal obstruction, it is not sufficient that the pain and vomiting should be relieved and the general physical condition improved; for unless the bowels are moved the drug is of no real value, but only masks the symptoms. Dr. H. Gebele[2] records a case of ileus in which atropine gave such temporary relief from pain and vomiting on the fifth day as to postpone operation, but upon the ninth day it was apparent that the only hope of saving life was to perform laparotomy. When the abdomen was opened a coil of the small intestine was found to be gangrenous and completely obstructed by inspissated feces. Enterotomy was performed, but the patient died. Gebele felt that in this case atropine masked the symptoms, and had an operation been performed upon the fifth day the chances for recovery would have been much better. I believe that the operation should have been undertaken twenty-four hours after the administration of atropine, as the bowels had not moved at that time.

Although the symptoms of *atropine intoxication* are extremely alarming, fatalities from this alkaloid are rare. Two recent cases of severe poisoning, in which very large doses were taken with-

[1] Therapeut. Monatshefte, February, 1902.
[2] Münchener med. Wochenschrift, 1901, No. 33.

out lethal effects, seem to illustrate this fact. M. Selo[1] reports the case of a boy, aged eleven years, who at a single dose took 0.05 gramme ($\frac{5}{6}$ grain) of atropine sulphate. No treatment was applied for three hours, at which time the symptoms of intoxication were very marked. Unsuccessful attempts to evacuate the stomach were made, and diluted vinegar was given by the mouth, and a clyster containing 0.5 gramme (7½ grains) of chloral hydrate. Recovery was complete and uneventful. Another case of atropine poisoning is reported by L. L. Beehler.[2] A woman, aged twenty-five years, took, with suicidal intent, 3 grains (0.18 gramme) of atropine sulphate, and was seen within twenty minutes after having taken the drug; $\frac{1}{10}$ grain doses of apomorphine repeated in fifteen minutes and $\frac{1}{8}$ grain after thirty minutes failed to produce emesis; 20 grains of copper sulphate were then administered without effect, and it was found impossible to pass a stomach-tube. Pilocarpine, hypodermically, failed to produce sweating, so it will be seen all of the atropine was absorbed. The only other drug employed was strychnine, $\frac{1}{40}$ grain, which was given at the beginning of treatment, and repeated once after fifteen minutes. Recovery was complete about the fourth day, the pupils remaining somewhat enlarged until the sixteenth day. The most striking feature in this case was the remarkable rise of temperature, which had reached 105° F. one and one-half hours after the onset of the symptoms, and 106° F. half an hour later.

Cacodylates. The salts of cacodylic acid, particularly those of sodium and iron, have, during the past two years, been employed quite extensively as substitutes for the arsenous acid, and the inorganic salts of arsenic. It was claimed that the cacodylates, while therapeutically active, were, even in quite large doses, non-toxic, and that they did not give rise to abdominal pains, diarrhœa, puffiness of the eyelids, or any of the symptoms of mild chronic arsenical poisoning. It was enthusiastically stated that in treating phthisis, chorea, anæmia, chronic malaria, and certain skin diseases these newer compounds were far superior to all inorganic salts and preparations of arsenic. Having employed sodium cacodylates for more than a year, our experience justifies us in stating that it may be used with benefit when arsenic is indicated; that it is far less therapeutically active and less toxic than the inorganic salts of arsenic, and when administered in full doses it may cause nausea, abdominal pain, and œdema of the tissues. In one case under treatment with 1-grain doses of sodium cacodylates (Merck's) three times a day there was marked œdema of the face, feet, and hands, after the patient had taken the remedy one week. On account of the

[1] Münchener med. Wochenschrift, No. 48.

[2] Journal of American Medical Association, April 26, 1902.

garlicky odor imparted to the breath, many patients object to it. This odor usually appears within twenty-four hours from the beginning of medication, and persists for several days after the drug is discontinued. It has been contended by some that if given hypodermically this unpleasant feature is avoided, but this is contrary to my experience. No doubt exists in my mind that the cacodylates possess therapeutic properties similar to other arsenical compounds, but the arsenic in them is so firmly combined with the methyl radical as to render it difficult of disintegration, and is therefore less active. I can hardly agree with Prof. Thomas A. Frazer,[1] who states that he was confirmed in his preconceived opinion that cacodylic acid is inert as a therapeutic or toxic substance. The urine of patients under treatment failed to respond to Reinsch's test for arsenic, except after long oxidation processes, and this leads Dr. Frazer to conclude that the arsenic is not eliminated from the radical, as the compound passes through the system, and that cacodylic acid is eliminated through the kidneys unchanged. In none of his cases was there puffiness of the skin. Edmund Saalfeld[2] used cacodylates with benefit in treating *psoriasis, lichen, acne, Duhring's disease, lupus, erythematosus,* and similar skin diseases. He says it does not prevent a recurrence in psoriasis, but rather shows a tendency to lose its power when given in successive relapses of the disease. In addition to digestive disturbances, he says dermatitis and toxic neuritis must be guarded against during cacodylic medication. The reports of Burlureaux[3] concerning the value of cacodylates in treating skin diseases are not favorable to the substance. Evoli[4] and P. Gallois[5] testify to the value of cacodylates in *tuberculosis.* Gallois[6] found the cacodylates most satisfactory in *chronic bronchitis* (accompanied by severe asthma) in elderly patients. Armand Gauthier[7] states that it is superior to quinine in the treatment of certain obstinate cases of *malaria.*

In addition to sodium cacodylate a number of other newer arsenic compounds have recently been introduced into medicine, the object of the originator of each salt being to produce an arsenic compound which would be less toxic, and, therefore, capable of being given in larger doses than arsenic acid, sodium arsenate, or any of the ordinary salts and preparations heretofore used.

ARRHENAL, the disodium methylarsenate, was introduced by A. Gauthier to take the place of the monosodium cacodylate. This com-

[1] Scottish Medical and Surgical Journal, May, 1902.
[2] Therapeut. Monatshefte, June, 1901.
[3] Annales de Dermat. et Syphil., March 15, 1902.
[4] Hospitals tidende, September 25, 1901.
[5] Bull. Générale de Therapeut., October 23, 1901.
[6] Bull. Méd., October 16, 1901. [7] Les Nouveaux Remèdes, 1902, vol. lxi. p. 529.

pound, unlike the latter salt, does not impart a garlicky odor to the breath or give rise to any digestive disturbances when taken by the mouth. It is said to be more therapeutically active, although no more toxic than sodium cacodylate.

It forms long prismatic needles, is freely soluble in water, insoluble in alcohol, and is decomposed by the application of heat.

A. Gauthier,[1] the originator of this compound, has used it with a considerable degreee of success in treating irregular forms of *malaria* which resisted the action of quinine. He also employed it with good results in treating *pulmonary tuberculosis, tubercular adenitis, chorea, pernicious anæmia, severe secondary anæmias, chronic skin diseases,* and *vomiting of pregnancy.* In chronic affections the maximum good was obtained by the administration of daily doses of about $\frac{1}{4}$ of a grain, although when the urgency of the case requires it, this dose may be greatly exceeded without fear of toxic effects. The best results seemed to be obtained when the remedy was administered continuously for five days, and then interrupted for five days. Special care must be exercised in administering the remedy to persons suffering from hepatic cirrhosis or congestion, or from cardiac disease, as well as to those subject to pulmonary or intestinal hemorrhages.

The compound may be prescribed in aqueous solutions, or administered in capsules. If a rapid effect is desired arrhenal may be dissolved in water and administered hypodermically.

℞.—Arrhenal . . . . . gr. vj.
Tinct. lavendulæ comp. . . . . f℥j.
Aquæ cinnamomi . . . . . q. s. ad. f℥j.
Misce. Sig.—Teaspoonful once daily.

℞.—Disodii methylarsenatis . . . . . gr. vj.
Pone in capsulas No. xii.
Sig.—One to two capsules daily.

℞.—Disodii methylarsenatis . . . . . gr. ij.
Aquæ dest. (steril.) . . . . . f℥j.
Misce. Sig.—Fifteen minims, hypodermically, once daily.

ATAXYL, or meta-anilid of arsenous acid, has recently been introduced by Dr. Walther Schild[2] as a substitute for the various official salts and preparations of arsenic. It appears in the form of a white, odorless powder, of a feebly salty taste, and soluble in water to the extent of about 18 per cent. It is said to contain about 37 per cent. of metallic arsenic, about half as much as is contained in arsenous acid. While very strong in arsenic, it is said that it may be administered in daily

[1] Bull. Académie de Méd. de Paris, February 22, 1902; Les Nouveaux Remèdes, 1902, vol. xviii. p. 73.

[2] Berliner klin. Wochenschrift, March 31, 1902.

doses of from one-half to three-fifths of a grain without giving rise to disagreeable features; but in single doses of six grains it gives rise to such unpleasant effects as chilliness, vertigo, headache, cardiac palpitation, and pharyngeal irritability, all of which subsided rapidly after the withdrawal of the drug. The remedy is not suitable for administration by the mouth, as small doses thus administered produce gastric disturbance.

Schild administered the drug to seventy-five patients suffering with the various skin lesions for which arsenic is considered valuable, and was favorably impressed with the results obtained.

Marked cardiac disease constitutes a contraindication to the use of the preparation, inasmuch as it gives rise to palpitation and dyspnœa even if administered in small doses.

IODO-MERCURIC-CACODYLATE is not a definite chemical compound, but a liquid made by dissolving 1 gramme of cacodylate of mercury, 2 grains of cacodylic acid in 75 grammes of distilled water, to which is added 1 gramme of sodium iodide, enough caustic soda to neutralize and enough water to make 100 c.c. This combination is said to contain in each c.c. 4.7 milligrammes of biniodide of mercury, 4.7 milligrammes of iodide of sodium, and 3 centigrammes of cacodylate of sodium.

This solution, which was originated by Brocq, Civette, and Fraisse,[1] has been employed hypodermically in average doses of about 2 c.c. in the treatment of *syphilis*. Comparatively little pain is experienced from the injection; there were few accidents occurring in the forty-eight cases treated. No exaggerated claims are put forward regarding the superiority of this preparation over other mercurials, but it seemed to be particularly indicated in syphilitic cases, when there is marked denutrition, loss of flesh, and neurasthenia in persistent secondary manifestations of the mucous membranes and skin, and when there are seborrhœic complications.

CACODYLATE OF MERCURY has been found too irritating for subcutaneous or oral administration.

CACODYLATE OF IRON OR ATARSYLE in doses of about $\frac{1}{4}$ to $\frac{1}{6}$ grain has been used, to a limited extent, in the treatment of *anæmia*, but seemed to possess no advantage over the arsenate of iron.

CACODYLATE OF MAGNESIUM has been employed as a substitute for sodium cacodylate, but is less soluble and no more active.

Cactus Grandiflorus. The contradictory results secured from the use of cactus grandiflorus are accounted for by Dr. J. R. Green,[2] by reason of the fact that there are great variations in the activity of

[1] Therapeutic Monthly, November, 1901; Bull. Therapeutique, 1902, No. 18; Annales de Dermat. (Paris), October, 1902.

[2] American Medicine, November 2, 1901.

different preparations. He claims that good results are only to be secured from a tincture made with strong alcohol from the fresh plant. Tinctures made with dilute alcohol should not be employed. It is also claimed that the valuable properties of the drug are lost in manufacturing the fluid extract.

Carbolic Acid. As a chemical antidote and eliminant in cases of carbolic acid poisoning, I regard the soluble sulphates as superior to all others. The use of alcohol in such cases has been freely discussed in these pages heretofore, and I still hold to the opinion that alcohol is neither a chemical antidote nor a physiological antagonist when the acid is taken internally. It is interesting to note that Ferreby[1] has employed caffeine as a physiological antagonist after having met with failure from the use of atropine and strychnine. Since the publication of Harrington's article, calling attention to the frequency of *gangrene* of the extremities from diluted carbolic acid dressing, there have been a number of other cases reported. A peculiar and interesting one is that of John S. Sheldon.[2] The patient, a man, was given a diluted solution of carbolic acid as a lotion to be used on the right foot. In preparing to use it according to directions, some was spilled on the left foot, and becoming alarmed, the man neglected to apply the lotion to the right foot. Five days later the left foot became numb, and by the eighth day painful. The patient then went to the hospital for treatment, and upon examination Sheldon found there was gangrene of the left foot and toes. The carbolic acid treatment of *tetanus* continues to be favorably reported on. Coley and Satterwaite[3] have found that in a great majority of the cases of *hydrocele* after evacuating the fluid an injection of 2 minims of crystallized carbolic acid liquefied with glycerin will cause obliteration of the sac. They do not believe the large quantities formerly advised entirely safe or necessary.

Cocaine as an Antidote to Morphine. In an article in the *Philadelphia Medical Journal,* March 9, 1901, discussing the physiological action of strychnine and its influence in cases of *opium-poisoning,* Dr. Edward T. Reichert called attention to the probable value of cocaine in treating cases of poisoning with morphine. Later Dr. Albert C. Barnes placed on record in the *Philadelphia Medical Journal,* December 21, 1901, a case of morphine poisoning successfully treated with cocaine, and in the *Therapeutic Gazette* of September 15, 1902, states that the case was treated in January, 1901, before the publication of Dr. Reichert's paper. In the *Therapeutic Gazette* of October 15, 1902, Dr. H. S. Hedges claims priority of the discovery for Dr. J. W. Strickler

[1] British Medical Journal, September 14, 1902.
[2] Medical Record, November 6, 1901.
[3] New York Medical Journal, March 29, 1902.

(now deceased), whom he states carried out a series of experiments upon the antagonistic action of morphine and cocaine in 1895 or 1896, and published his results (he believes) in the *New York Medical Record*. Recently Dr. Reichert[1] has published the results upon the antagonism existing between the alkaloids—morphine and cocaine.

The case of Dr. Barnes was an extremely interesting one, inasmuch as many of the methods usually employed in opium-poisoning had been resorted to without avail, and the hypodermic use of cocaine saved the patient's life. When first seen by Dr. Barnes, the patient, a young woman, had been unconscious for an hour and showed all the symptoms and physical signs of profound opium-poisoning. One-half grain of cocaine hydrochlorate was immediately administered hypodermically. As no marked improvement was noted after half an hour, the same dose was repeated, and ten minutes later the beneficial effects of the remedy were plainly evident. The pulse and respiration improved, and there were signs of returning consciousness. As the improvement was not marked enough to indicate sufficient stimulation, another dose of one-fourth grain was injected, and within ten minutes consciousness returned, and the pulse and respiration became satisfactory. Within a half-hour after the last injection the girl developed a noisy delirium, the heart-beats registered 180 to the minute, her respirations were quick, short, and jerky, and she had tonic and clonic movements of the arms and legs. The case was now one of cocaine-poisoning of the first stage, and fearing the after-depressing effects of the drug, a half-grain of elaterin was given to promote elimination. Four hours after the last dose of cocaine was given the patient again developed symptoms of stupor, with slow pulse and respiration; but these were successfully combated by strong coffee, forced involuntary movements of the arms, etc. The patient was under his observation from 11 A.M. to 5 P.M., at which time, at her own request, she was removed to a hospital, where it was learned later that she had entirely recovered from the poison. She had received during a period of about seventy minutes a grain and a quarter of cocaine hydrochlorate, which was evidently an excessive dose for this patient; but a review of the case makes it evident that by the use of cocaine her life was saved. The recent paper of Dr. Reichert[2] presents the results of an exhaustive research in which is pointed out the antagonistic action of *therapeutic* doses of cocaine and *toxic* doses of morphine upon the circulation, respiration, temperature, nervous system, and metabolism. The paper leads to the conclusion that the antidote should be used with care, as in cases of opium-poisoning it would not be difficult to administer an overdose. He states that the effects caused

[1] Therapeutic Gazette, July 15 and August 15, 1902 [2] Loc. cit.

by a given dose of cocaine per kilo of body weight vary in intensity within wide limits, and that the typical cocaine effect may be delayed in morphinized animals, and then appear with marked intensity, as shown by the increase of heat production, bodily temperature, and motor excitation at a time when in normal animals they are lessening rapidly. Under such conditions the dangers of morphine-poisoning may be superseded by those of cocaine-poisoning. In addition to these facts, it is noted that cocaine has a tendency to cause syncope in some individuals, and, therefore, in cases of opium-poisoning, it should be administered cautiously in small repeated doses, instead of in full doses at longer intervals.

Coley's Fluid. *Mixed Toxins of Erysipelas and Bacillus Prodigiosus.* Although Coley's fluid has been in use for nearly ten years, it cannot be said to have yet passed through the experimental stages, and there is still a great diversity of opinion as to its usefulness in treating sarcomata.

In 1884, after observing the wonderful effect of an accidental inoculation with erysipelas in a case of sarcoma of the neck, and it having been previously noted by others that attacks of erysipelas greatly modify or caused the disappearance of sarcomatous growths, Dr. William B. Coley was led to experiment with the toxins of erysipelas in treating cases of inoperable *sarcoma.* The results of his experiments ultimately led to the production by him of a fluid containing the toxins of streptococcus of erysipelas and bacillus prodigiosus.

To be of maximum effect, Coley tells us that the value of all preparations of the toxin depends largely upon the virulence of the original cultures. He recommends that the fluid should be tried only in cases of inoperable sarcoma. At the beginning of treatment, about one-half minim of the unfiltered or a minim of the filtered toxins should be injected daily into or about the tumor, and the dose increased each day until the reaction temperature reaches 103° F. or 104° F.

In estimating the dose, however, the temperature should be the guide; unless the reaction is obtained little benefit is likely to follow the injections.

If well borne the treatment may be continued three or four weeks, after which time, if there is no marked improvement, it should be discontinued.

In some successful cases the treatment has been continued for several months, with occasional intermissions of a few days. In other cases it has been applied intermittently at intervals of several months for a year or two.

The application of the fluid is attended with some risk, such as collapse from too large doses. This is especially so when injected into a

very vascular tumor, or from insufficient care as regards asepsis, in the presence of a granulating or sloughing surface. Since the introduction of this agent a number of cases have been reported as cured, and a number for a time benefited, while, of course, there have been many failures. The best results have been obtained in treating the spindle-celled variety of sarcoma; while no success can be said to have followed its use in cases of the melanotic variety.

Creosote Carbonate. During the past year several writers have testified to the value of creosote carbonate in the treatment of *croupous pneumonia.* In nine cases reported by L. Weber,[1] who employed the drug in doses of from 8 to 10 grains five times a day, remarkably good and uniform results were obtained. After a drachm or more had been taken, there was usually a drop in the temperature and amelioration of the other symptoms. If the remedy was discontinued after that time the temperature would again rise, but if continued the disease was kept under control, and in all cases except one (which terminated fatally from myocarditis during convalescence) recovery was rapid. He does not believe the drug is an antipyretic nor a bactericide, but attributes its beneficial influence to its antidotal power to the pneumotoxin. In his experience the drug was not a depressant nor gastro-intestinal irritant. He expresses a preference for the following combination:

℞.—Creosoti carbonatis . . . . . ʒij.
Saponis medicat. . . . . q. s.
Misce et pone in capsulas No. xxiv.
Sig.—Two to be taken every three hours; ten to twelve daily.

Dr. J. L. Van Zandt[2] states that after an experience of seven years he has come to regard the remedy as highly valuable in treating pneumonia. For adults, from 7 to 10 grains should be given every three hours, or (in severe cases) more frequently for a few doses; and in some instances single grain doses are beneficial. The remedy must not be discontinued as soon as the fever and other symptoms subside, but should be continued for three or four days longer. Guaiacol is not, in his estimation, a suitable substitute for the creosote carbonate. He states that the remedy is best administered by stirring it in a little hot, sweetened water, to be swallowed during agitation or in simple emulsion, as it is not soluble in aqueous liquids. It should not be compounded with acids or alcohol, as these substances develop the taste of creosote. The remedy is spoken of favorably by Dr. H. W. Cummings,[3] who

[1] Medical Record, November 2, 1902.
[2] Southern Practitioner, December, 1901.
[3] Texas Medical Journal, December, 1901.

states that he has successfully treated twenty cases of pneumonia with it. He claims that it modifies the fever, lessens the severity of the cough and pain, and seems to act beneficially in other ways. Eighteen cases of pneumonia (with one death) treated by creosote carbonate are reported by Dr. W. H. Thomson.[1] In this series the disease terminated by lysis in twelve cases, and by crisis in only five—two being mild cases. The doses recommended by this author are 15 grains every two hours, day and night. He has never noted any depressing effect upon the circulation, or irritation to the kidneys, and he suggests the following formula :

℞.—Creosoti carbonatis . . . . . ʒiv.
Glycerini . . . . . fʒj.
Aquæ menthæ . . . . . q. s. ad. ʒiij.
M. Sig.—Dose. Tablespoonful in water.

Dr. Andrew H. Smith[2] considers the remedy a specific in pneumonia.

Although these and other recent reports are most favorable to the use of creosote carbonate in treating croupous pneumonia, we should not forget that the disease is self-limited, and that scarcely a year passes that some agent is not brought forward and highly lauded as a cure, only to fall into disuse and be succeeded by others.

Crurin. Chemically this substance is a quinolin bismuth sulfocyanide. It was originally used in treating leg ulcers, but more recently has been employed by E. Jacobi[3] in the treatment of *gonorrhœa*. Its probable value in this affection was suggested from a knowledge of the fact that when added to water the compound decomposes into bismuth sulfocyanide, an astringent, quinolin sulfocyanide, and free sulfocyanic acid, which is an active bactericide. By the use of the formula given below the discharge was readily controlled, and gonococci disappeared more rapidly than from the use of other astringents and antiseptics. Jacobi advises that the injections should not be stopped as soon as the discharge ceases, but should be persisted in for some days.

In *gonorrhœal cervicitis*, urethritis in the female, the remedy was made into bougies with cacao butter and applied.

For Injections.

℞.—Crurin	gr. xv.	1 gm.
Glycerini	fʒjss.	5 gm.
Aquæ	fʒvijss.	200 gm.

Misce. (Shake well.)

Sig.—About two or three drachms to be used by injection three times a day.

As commercial crurin contains about 25 per cent. of (added) starch, in making the emulsion the powder should first be rapidly triturated

[1] Medical Record, February 1, 1902.
[2] Ibid., March 15, 1902.
[3] Deutsche med. Wochenschrift, December 26, 1901.

with the glycerin, mixed with an equal quantity of water, and the balance of the water slowly added.

For gonorrhœal cervicitis or urethritis in females:

℞.—Crurin . . . . . gr. iij.
Olei theobromatis . . . . . ʒjss.
Misce ft. bougie No. vi.
Sig.—Insert a bougie twice daily.

Cuprol. This new salt of copper is offered as a substitute for copper sulphate in the treatment of *chronic conjunctivitis.* It was originated by Dr. Schwickerath, of Bonn. Cuprol is a copper nucleid containing about 6 per cent. of copper. It is readily soluble in water; but, on account of its tendency to decompose, solutions are best kept by the addition of a small quantity of chloretone. Ten per cent. solutions have been found to be about the proper strength for general use. Its application is only slightly painful and gives rise to very little irritation of the tissues.

Digitalis. From the fear of its cumulative action many physicians hesitate to administer digitalis for longer than a few days or weeks at a time. These fears are not altogether groundless, especially when full doses are being employed, or if the emunctories are not active; but there are cases with weak hearts in which almost continuous administration of the remedy is necessary to sustain a proper condition of the circulation.

Jacobi states, as his experience, that in bad cases of dilatation of the right heart, with cyanosis and orthopnœa, one, two, or three full doses of digitalis given at intervals of three or five hours will contract the heart and restore pulmonary and general circulation, while in chronic conditions of weak heart of either muscular or nervous origin, or of insufficient action caused by pulmonary obstruction, small doses of the drug are required for months or even years, and may be given without hesitation. When given over long periods of time, it is, of course, necessary to regulate the dose and the interval of administration. The heart, in many cases, requires daily stimulation, and patients taking digitalis in the proper way do not show cumulative effects, nor do they become so accustomed to its influence as to lose the benefit of its action.

For long-continued administration he expresses a preference for the solid extract, in doses of about ½ grain, three times a day, combined in pill form with sparteine, strychnine, arsenic, or other drugs, as the case may require.

In tubercular cases with weak hearts it has been his custom for years to prescribe such doses as have been stated above, and continue for long periods of time without fear of untoward effects. In many

instances patients were seen only at long intervals. Very little care is required to avoid disagreeable results, as cumulative effects are either the consequence of excessive or too frequent—unnecessarily frequent—doses, or of the selection of the improper preparation. The infusion, tincture, or solid extract are preferred. On account of being well borne by the stomach, the solid extract, he believes, as a rule, to be the best preparation for long continuous use.

As to the advisability of using digitalis in cases of *aortic insufficiency*, he believes that if discovered early, before compensation has been greatly disturbed, small doses continued for a long time will be of permanent value, but in old cases with considerable venous obstruction, the drug will fail to give relief.

Jacobi dwells upon the value of digitalis not only in those cases classed strictly as heart diseases, but also in other chronic diseases and conditions which have a depressing influence on all parts of the organism, and in which the heart is not the least to suffer.

He considers it a valuable tonic along with iron, arsenic, and strychnine in cases of general *anæmia* and slow convalescence, as in such cases it not only acts as a tonic to the heart muscle, but through its stimulating effect upon the whole circulatory system, assists in nutritive changes throughout the body. In conjunction with other appropriate remedies he considers it of the very greatest utility in all cases of *chlorosis*.

Dr. H. A. Hare[1] deplores the tendency of many physicians to institute stimulating treatment immediately upon the discovery of valvular heart lesions, without giving due consideration to the condition of the heart muscles or capillaries, or before carefully studying the state of the arterial tension and renal functions. He is convinced that in many cases with valvular heart lesions, stimulants are not required, while in others the doses administered are frequently in excess of the requirements, and are often given for unnecessarily long periods.

For some cases full doses are necessary for a short time at the beginning of treatment, but in most instances they should be rapidly and considerably diminished. He has been surprised to find how much good could be produced by one or two minims of an active physiologically tested tincture of digitalis given three or four times a day, the patient at the same time being required to rest.

In myocardial weakness with high arterial tension, the value of digitalis is often enhanced by combining it with nitroglycerin; while in some cases of hypertrophy with irregularity of the pulse and heightened arterial tension, even though complicated by valvular lesions, are benefited by well-balanced doses of digitalis with aconite.

[1] Therapeutic Gazette, August 15, 1902; Journal of American Medical Association, September 27, 1902.

Hare states emphatically that digitalis is not always the proper heart stimulant, even in some cases of valvular lesions with myocardial weakness, for although the drug usually improves the nutrition of the heart muscle, degenerative changes in the coronary arteries may be so great as to nearly close them and render it impossible for the heart to send an increased blood supply through these vessels.

In still other cases the degenerative changes in the heart muscle are so extensive that it is impossible for digitalis to improve its nutrition, while driving the remaining healthy fibres to an endeavor far in excess of their ability. As is well known, the heart receives its blood supply through the coronary vessels, but Hare calls attention to the recently discovered physiological fact that it also receives part of its nutrition from the blood flowing through the foramina of Thebesii, and in some cases with very advanced changes in the coronary arteries the heart may receive its nourishment chiefly in this way. It is possible to conceive that under these circumstances digitalis may be useful even in such cases.

It is true that one of the active principles of digitalis, digitonin, depresses the heart, but it is equally true that the drug as a whole stimulates the heart muscle and improves its nutrition.

I think the assertions of Dr. Porter,[1] that the drug is heart muscle poison and that it decreases the nutrition of the heart, are untenable.

It seems unfair to state that when "administered in homœopathic doses, no perceptible deterioration of the heart will appear, but when a thorough reliable preparation of digitalis is used, and the drug is administered continuously up to the full physiological limit, the heart is invariably damaged," for at the present time no intelligent therapeutist uses the drug in either of these ways, but administers such doses as to secure the therapeutic and not the toxic action.

The value of digitalis in mitral stenosis and insufficiency, with dilatation of the ventricle, is admitted. Porter holds that it should be given only for a few days at a time, at the longest. It should only be given to influence the heart and circulation when the arteries are very much relaxed, and the pulmonary or systemic veins are overfilled with blood. Outside of these narrow confines he considers the use of the drug, to say the least, extremely poor therapy. While admitting the value of a few full physiological doses of the drug, he condemns its administration for prolonged periods. The combination of digitalis with nitroglycerin, he states, may lessen the damaging effect by diminishing the increased work forced upon the heart, but it does not relieve the heart altogether of the extra strain put upon it by digitalis, nor does it antidote the toxic effects of that drug upon the involuntary muscles. So

[1] Medical News, May 3, 1902.

sure is he of the power of digitalis to lessen the nutrition of the heart-muscle that he states that, theoretically, it should be useful in cases of cardiac hypertrophy.

Practically, however, he considers the remedy dangerous in this condition. The so-called cumulative effects of digitalis he believes to be due to the continuous administration of excessive doses, which, in the end, result in poisoning, due to its diminishing the nutritive supply to the cardiac muscle resulting from high arterial tension, to the increased work imposed upon the heart, and to the action of digitalis *per se* as a decided muscle poison.

Dionin: Mono-ethyl-ester Morphine Hydrochloride. This comparatively new morphine derivative has now been in general use for a sufficient length of time to enable us to form a fair estimate of its value as a substitute in some cases for morphine.

There seems little reason to doubt its sedative and analgesic properties, both of which, in my opinion, are less powerful than morphine, but more pronounced than codeine. While nausea and headache do sometimes follow full doses, they are far less common than with morphine, and it is almost entirely devoid of constipating effect, and has little tendency to check bronchial secretions. The remedy has been extensively employed in expectorant mixtures, and also in *pertussis* for the purpose of controlling harassing cough. It has also been used to a limited extent as a local application to relieve deep-seated pain in the eye, in earache, and also in toothache from caries. The strength of solutions employed for such purposes ranges from 1 per cent. for instillation into the eye to 3 per cent. for local application within the tooth cavity.

The usual dose of the drug is from $\frac{1}{6}$ to $\frac{1}{3}$ of a grain, three or four times a day for adults, and $\frac{1}{50}$ to $\frac{1}{20}$ of a grain for children of three to ten years of age. Its chemical and pharmaceutical incompatibilities are practically the same as for morphine salts.

The following formulæ are suggested for internal administration to adults suffering with *bronchitis:*

℞.—Dioninæ . . . . . gr. iv.
Terpin. hydratis . . . . . gr. xxiv.
Syrup. tolut. . . . . f℥j.
Elix. aromat. . . . . q. s. ad. f℥iij.
Misce. Sig.—(Shake.) Teaspoonful every three hours.

℞.—Dioninæ . . . . . gr. iv.
Essenciæ pepsini . . . . . f℥ iij.
Misce. Sig.—Teaspoonful every three or four hours to quiet cough.

℞.—Dioninæ . . . . . gr. iij.
Creosoti carbonatis . . . . . ℥ij.
Misce et pone in capsulas No. xxiv.
Sig.—Take one capsule three times a day.

Diphtheria Antitoxin. It is no exaggeration to state that the specific value of diphtheria antitoxin in the treatment of diphtheria is almost as firmly established as that of quinine in malaria. When the antitoxin is employed upon the first day of the disease recovery is almost invariably rapid, sequelæ are infrequent, and unfavorable results extremely rare. When deferred until the second or third day, the effects are less remarkable; and after that time, although it is considered the best treatment to be pursued, its curative effects are still less marked. The recent report of Professor Lewis Woodhead (a summary of which appears in the *British Medical Journal*, September 21, 1901, and in the "London Letter" of the *Therapeutic Gazette* of the same year) upon the bacteriology and antitoxic treatment of 12,172 cases of diphtheria patients admitted to the hospitals of the Metropolitan Asylums Board in 1895 and 1896 covers a great number of carefully studied cases, and "will form a standard of comparison for future work by which may be gauged improvements in treatment and in the results obtained that may be of inestimable value." The methods of antitoxic treatment have been improved, and the death-rate correspondingly decreased since these cases were under observation. The report, however, illustrates the great life-saving properties of the antitoxin from the very beginning of its adoption. Soon after the remarkable clinical reports of Roux in 1894, the mortality-rate in these institutions for children under five years was 47.4 per cent., which, under antitoxic treatment in 1895 and 1896, fell to 31.52 per cent. Under antitoxic treatment in 1895 the mortality-rate in faucial diphtheria was 12.1 per cent.; when the fauces and nares were affected, 39.5 per cent.; fauces and larynx, 37.3 per cent.; larynx only, 30.5 per cent.; fauces, larynx, and nares, 62.2 per cent. With improved methods in 1896 there was a lower percentage of fatalities in these severe cases. When the larynx and nares were affected and antitoxin withheld the mortality-rate in 1895 was 82.6 per cent., and in 1896, 64.2 per cent. In tracheotomy cases without antitoxin, the mortality-rate in 1894 was 70.4 per cent., while in 1896 with antitoxin, the death-rate was reduced to 41.46 per cent. Estimates based upon the smaller number of cases, and the reduced death-rate where tracheotomy was required, leads to the conclusion that 225 of these cases were saved in a single year by antitoxin. More recent statistics from the Brooks Hospital (taken from the annual report of the Hospital Committee of the Metropolitan Asylums Board for 1900) show the mortality-rate for patients under five years of age to have been reduced to 15.6 per cent., and for cases after tracheotomy to 33.7 per cent. These reports also show the great advantage of early antitoxin treatment; for instance, at the Brooks Hospital, during 1900, 854 cases of diphtheria were treated with antitoxin; of these 31 were

treated on the first day without a single death ; 249 on the second day, with a mortality-rate of 3.6 per cent. ; 238 on the third day, with a death-rate of 6.7 per cent. ; 161 on the fourth day, with a death-rate of 14.9 per cent. ; and 175 on the fifth and subsequent days, with a death-rate of 21.2 per cent. The value of the antitoxin treatment in the Municipal Hospital of Mulhausen[1] (Germany) is shown by the following record : The percentage of mortality in diphtheria in the pre-antitoxin years, 1892, 1893, and 1894 was 53.4 per cent., 55.3 per cent., and 51.7 per cent, respectively ; while in 1895, 1896, 1897, 1898, 1899, and 1900 (since the introduction of antitoxin) the death-rate has been reduced to 38.5 per cent., 28.8 per cent., 16 per cent., 20 per cent., 15 per cent., and 18.7 per cent. There was also a corresponding decrease in the number of cases requiring tracheotomy, and improvement in the death-rate of such cases. That the favorable results were not due to an especially mild form of the disease is shown by the fact that during the years of 1899 and 1900 the cases were more severe than at any time for the past twenty years. E. Müller,[2] of Berlin, gives a statistical report showing the remarkable decrease in the death-rate from diphtheria in Germany since serum treatment was introduced. He believes that statistics covering a period of twelve years, and with a population of ten millions of people, cannot be ascribed to casual circumstances. The results of antitoxin treatment of diphtheria in the City Hospital of Glasgow during six and one-half years is reported by John Brownlee.[3] The death-rate for all ages has been greatly lowered, and it has been especially noted that improvement has been more marked as the age period increases from one to ten years. A. Stanley[4] reports a series of 500 cases of diphtheria treated with antitoxin, showing a death-rate of 16 per cent. In addition to these statistical reports, great numbers of writers continue, through the medium of medical journals, to express their entire satisfaction with the antitoxin treatment and their conviction of the great advantage to be secured by the early application of the remedy. Whenever there is doubt as to the existence of diphtheria, the remedy should be immediately applied, and the diagnosis determined later. It is undoubtedly true that skin eruptions, joint pains, and a mild rise of temperature often follow injections of antitoxin, but ill-results traceable to such infections are very infrequent. The remedy has probably fewer untoward effects than any other active remedial agent. In Stanley's 500 cases eruptions occurred in 112 cases, as follows : erythema, 58 ; erythema and urticaria, 15 ; urti-

[1] Editorial, Journal of American Medical Association, April 19, 1902.
[2] Jahrb. f. Kinderheilk., February, 1902.
[3] Glasgow Medical Journal, 1902.
[4] British Medical Journal, February 16, 1902.

caria alone, 30 ; scarlatiniform, 6 ; morbiliform, 3 ; and transient early erythema and urticaria (usually at the site of inoculation), 17. The onset of erythema varied from the fourth to the twenty-ninth day, and of urticaria from the fourth to the nineteenth day. He states that the typical diphtheria antitoxin eruption is a marginate erythema on the psoriasis surfaces, tending to run in arcs of a circle. It usually lasts about three days, and is accompanied by slight malaise, and a rise in temperature. The eruptions appeared to be more frequent after the use of large bulks of serum than from the employment of small bulks of concentrated serum, and, therefore, appear to be due to the serum rather than the antitoxin. Dr. James J. Walsh[1] observed a case of *urticaria* in a girl, about twelve years of age, suffering from a mild form of diphtheria not treated with antitoxin, in which the eruption appeared on the fourth day. He considers it a mistake to attribute to the remedy all skin lesions appearing upon the body during treatment with antitoxin, and he thinks they are no more frequent after large doses than when small doses are employed, quoting the results of treatment with large and small doses from the New York City Board of Health, Drs. John H. McCollum and Frederick Grant Burrows. He believes that a careful study of the conditions produced by diphtheria itself will relieve the serum of some of the accusations made against it, and also that the same arguments may be applied to the assertion that the serum gives rise to albuminuria. Woodhead thinks that joint pains and rashes, while more frequent after antitoxin injections, are of trifling importance, but that cases of nephritis and adenitis are less frequent and the death-rate in cases of post-diphtheritic paralysis is slightly reduced. Upon the other hand, P. Geffrier and E. Rozet[2] assert that large doses of antitoxin aggravate renal symptoms and increase the frequency of rashes, and better results may, as a rule, be secured after the use of small doses. This theory is not at all in accord with McCollum's, Burrows', and others, who have shown beyond a reasonable doubt that very large doses are required to save the life in some patients. The duration of immunity after prophylactic injections of diphtheria antitoxin is said by Henry D. Jump[3] to last about three weeks, by Netter[4] three to four weeks, and by Sevestre[5] not longer than three or four weeks.

They all agree that, even though the injection is given, disinfection and isolation are necessary.

[1] Philadelphia Medical Journal, October 12, 1901.
[2] Archives de méd. des enfants, February, 1902.
[3] Philadelphia Medical Journal, January 11, 1902.
[4] Bulletin de l'Académie de Méd., March, 1902.
[5] Bulletin Médicale, March 19, 1902.

Diphtheria antitoxin by the mouth has been extensively employed by Dr. D. Montgomery Paton,[1] of Melbourne, Victoria, for the past three and one-half years, as a specific for streptococcus and staphylococcus infections in all their varieties, and for simple inflammations, traumatic and otherwise. He states that it has no parallel in medicine as an absorbent of inflammatory tissues, and that it has great power for good in some depressed nervous conditions, probably due to an acquired septic state or to autotoxæmia. He holds that gastric secretion has little or no effect upon antitoxin, and that after its exhibition by the mouth, skin eruptions, similar to those from subcutaneous injections, have been observed. He believes that when given hypodermically it is a specific for the toxins of diphtheria bacilli, and feeble in its action upon septic organisms; but when given by the mouth it is a specific for the staphylococcus and streptococcus, and weak in its action upon the Klebs-Loeffler bacilli. Some of the diseased conditions in which the remedy has been successfully used by him are erysipelas, peritonitis, appendicitis, acute rheumatic polyarthritis, puerperal infection, secondary infection in phthisis, traumatisms, abscesses, and suppurations. The dose usually employed in adults was ½ ounce (750 units) every six to twelve hours, and about half this quantity for children. We have not seen any confirmation of these statements in our reading.

Ethyl Chloride. Members of the medical profession seem to be ever on the alert to find an anæsthetic which may be used in the place of ether or chloroform, and at this time many are advocating the use of ethyl chloride as a general anæsthetic for the performance of short operations.

While reports of its successful use are becoming more numerous, we cannot but feel that with nitrous oxide for short operations, which may be performed within thirty to ninety seconds, ethyl bromide for operations lasting two to five minutes, chloroform and ether for long operations, we are quite well supplied with this class of drugs, and that when our experience with ethyl chloride becomes more extensive it will be found to possess no advantages which may not be secured from anæsthetics already well understood. Furthermore, it may be found to have disadvantages not now known.

The advantages claimed for ethyl chloride as a general anæsthetic are that by inhalation of very small quantities, general anæsthesia may be secured in a few seconds, that recovery is rapid, that it is safe, that it produces only slight changes in the pulse and respiration, and that disagreeable after-effects are infrequent.

To obtain good results the anæsthetic must be administered with

[1] Therapeutic Gazette, February 15, 1902.

admixture of air by means of a closed inhaler, which fits closely over the mouth and nose. The most satisfactory inhaler is one placed upon the market by one of the principal manufacturers of the anæsthetic fluids. It is so arranged that a glass tube containing the chloride may be so attached as to spray the liquid upon a sponge fixed in the inhaler which fits tightly over the nose and mouth. If such an inhaler cannot be secured or is not desired, the anæsthetic may be given from a cone or, from what is still better, a funnel, into the apex of which is fitted a sponge or piece of cotton. The base of the funnel should be placed over the mouth and nose, air excluded by holding the hands about it, and the anæsthetic sprayed upon the sponge or cotton through the small end of the funnel from a tube filled with the liquid.[1]

With from two to five cubic centimetres of the fluid administered in this way, general anæsthesia comes on within fifteen to sixty seconds, and lasts from two to five minutes. If somewhat more prolonged anæsthesia is desired, a larger quantity of anæsthetic may be administered as a single dose, or it may be re-administered. The anæsthetic is most suitable for short operations, but it has been successfully employed by the continuous inhalation method for periods of fifteen minutes. In quantities of from 2 to 5 centimetres, ethyl chloride is said to have little or no depressing action upon the circulation or respiration, and to be comparatively free from disagreeable after-effects, but we notice that reports are already beginning to appear stating that nausea, vomiting, and headaches are not infrequent after its administration. After inhalation of small quantities (2 to 5 c.c.) muscular rigidity and reflexes may or may not be abolished, but when large quantities (10 to 20 c.c.) are employed, reflexes and rigidity are, as a rule, entirely abolished. Sleep comes on without a primary period of excitement, and subjects come out from the influence of ethyl chloride and awaken promptly.

Alcoholic subjects do not take the anæsthetic well. No reliable statistics can as yet be given as to the percentage of deaths likely to occur during the use of ethyl chloride as a general anæsthetic.

Gelatin. It appears to be an established fact that subcutaneous injections of gelatin increase the coagulability of the blood. It has been asserted that the same effect may be secured by its administration by the mouth or rectum, and the experiments of H. C. Wood, Jr.,[2] show that digestion does not destroy its blood-coagulating power. Both digestion and high heat are said to liquefy and prevent re-jellying, and in view of the number of cases of tetanus (recently reported) after gelatin injec-

[1] Hare's Practical Therapeutics, ninth edition, p. 231.
[2] American Medicine, May 3, 1902.

tion, and the demonstration of tetanus bacilli in samples of gelatin, it is interesting and valuable to know if gelatin previously heated to a high temperature still retains its hæmostatic effect.

During the past year the remedy has been extensively employed in treating *hæmoptysis, hæmatemesis, hæmaturia, hæmophilia,* and *purpura hæmorrhagica,* but the most striking cases reported are those of A. Holtschmidt and M. Döllner in treating cases of *melæna neonatorum.*

Holtschmidt[1] used for five infants 15 c.c. of 2 per cent. solution, injected in two places. In three cases improvement was immediate, while one case required a second injection, and one a third before the cure was complete. Döllner[2] injected 40 c.c. of a 2 per cent. solution in five hours. The symptoms rapidly subsided, and the patient promptly recovered.

The administration of gelatin by enteroclysis, as recommended by Rocchi, is favored by Sereni,[3] who holds that the hæmostatic effect may be noted within ten minutes after the administration, and lasts for about six hours. He reports two cases of purpura hæmorrhagica successfully treated by this method.

Guaiacol. Dr. E. Grande[4] employed guaiacol as a local application over the parotid gland with considerable success in treating *mumps.*

The remedy was applied in the form of a 5 per cent. ointment, rubbed well over the parotid gland several times a day, and covered with a layer of carbolated cotton, held firmly in place with a bandage. In the twelve cases treated patients usually stated that pain was diminished after the third application, and the swelling rapidly subsided. The good effects were thought to be due not wholly to the analgesic action of the guaiacol, but upon the buccal mucous membrane through inhalation.

Haffkine's Prophylactic Vaccine against Plague. The presence of bubonic plague in the Philippine Islands lends new interest to the methods for the prevention and cure of this dreaded disease. The hygienic measures necessary to prevent the spread of the infection have been fully discussed in PROGRESSIVE MEDICINE heretofore, and attention has also been called to the specifics employed for inoculating against the disease and for treating already existing cases. It will be recalled that Haffkine's vaccine consists of a fluid containing the products of bacterial growth, and is employed by subcutaneous injections as a prophylactic against the disease. The dose advised is 1 to 5 c.c., according to age, and repeated once in about fourteen to twenty days after the first inoculation. The protective influence of the vaccine is

[1] Münchener med. Wochenschrift, January 7, 1902.
[2] Ibid., May 27, 1902.
[3] Il Policlinico, 1902, vol. vii., No. 46.
[4] La Semaine Médicale, 1902, No. 34.

said to last for at least six months. Numerous writers who have employed it attest its value. It is believed by J. Pinto[1] that the vaccine was of decided value during the recent epidemic of plague at Campos, Rio Janeiro. Although many of the cases were exposed to infection by contact with others, only two persons out of 1803 vaccinated developed the disease. One of these showed symptoms immediately after vaccination, so that in reality only one failure should be recorded, as the other individual was in the period of incubation when vaccinated. In one district the only person who contracted the disease was one who refused vaccination. The protective value of the vaccine and its freedom from ill-effects in those incubating the plague are pointed out by Alice M. Corthorn,[2] who states that in 1899 there were 147 cases of bubonic plague, with 109 deaths among the police of Poona, India; while early in the epidemic of 1900 the whole force was inoculated, with material benefit. Prior to inoculation there had been seven cases and six deaths. After inoculation there were seven cases and two deaths. Two of those developing the disease were in the period of incubation when inoculated, and both recovered.

Hedonal. Methyl-propyl-urethan. For *insomnia*, not of a severe type, accompanying neurasthenia, hysteria, general debility, and during convalescence after exhausting diseases, such as typhoid fever or pneumonia, hedonal acts very satisfactorily. In moderate doses of from 15 to 30 grains it is almost entirely devoid of any depressing effect upon the circulation, does not disorder digestion, and patients awaken from its influence without a feeling of drowsiness or hebetude.

The remedy is not a powerful hypnotic and is unsuited for severe cases of insomnia, or those cases complicated with wild delirium or mania. For insomnia in patients suffering with pulmonary tuberculosis, D. C. S. Reisman[3] found the drug useful. It was rapid and reliable in its action, free from after-effects, a sedative to bronchial sensitiveness, and free from the danger of creating a drug habit.

On account of its sparing solubility in water, and its disagreeable taste, it is best administered in cachets or capsules.

Hermophenyl, Hemophenol, Mercury-phenol-disulfonate of Soda. This is one of the newer compounds of mercury which is put forward as an antiseptic and antisyphilitic. It is not precipitated by albumin, nor decomposed by alkalies, hydrochloric acid, or ammonium sulphide.

In the strength of 1 per cent. solution, is said to be a powerful antiseptic, and being less irritating than other mercurials, in the strength of

[1] Brazil Medico, January 23, 1902.
[2] British Medical Journal, January 25, 1902.
[3] Buffalo Medical Journal, October, 1902.

1 : 500 can be kept in contact with the skin for prolonged periods or used hypodermically without giving rise to irritation or abscess formation.

As it may be heated to 248° F. (120° C.) without decomposition, gauze may be doubly sterilized by dipping into a solution of the antiseptic, and then subjected to heat.

It is freely soluble in water.

Reynes[1] employed the salt by hypodermic injections in treating *syphilis*, and expressed himself as satisfied with the results.

The following formula, of which the dose, 1 drachm, represented $\frac{1}{8}$ grain of metallic mercury, is suggested:

℞.—Hermophenyl . . . . . gr. ¾.
Aquæ destillatæ . . . . . f℥ ijss.
Misce. Sig.—One drachm by hypodermic injection at intervals of two to four days.

Heroine Hydrochloride (Morphine-diacetyl Hydrochloride). Judging from the numerous favorable reports, heroine hydrochloride has become popular as a sedative for allaying irritable coughs and as an anaphrodisiac and local anæsthetic. The asserted advantages of this remedy over morphine are that it is less likely to cause nausea or vomiting, it does not produce constipation, does not check bronchial secretions, and is a mild stimulant instead of a depressant to the respiratory centres. When used in doses of from $\frac{1}{24}$ to $\frac{1}{12}$ grain, the remedy does seem to be devoid of many of the by-effects of morphine, but when given in doses of $\frac{1}{6}$ grain or more, nausea, vomiting, and general hebetude have, in my experience, been as great as with morphine.

C. R. Marshall[2] concluded, from his experiments upon animals, that in both heroine and dionine the conclusive effect of morphine is increased at the expense of the sedative effect. He considers heroine more toxic, more convulsive, and less depressing to the respiratory centre than morphine. He holds that in appropriate doses it can prolong and increase the depth of inspiration, but the limits of its beneficial action are soon passed.

As an *anaphrodisiac*, A. Strauss[3] was well satisfied with the action of heroine, particularly in young men having frequent nocturnal pollutions, followed by headache and backache in the morning, to prevent painful erections during attacks of acute and chronic gonorrhœa, and after phimosis operations. He advises doses of about $\frac{1}{6}$ grain at bedtime, and states that it seems to act particularly well when administered in suppositories. As a local analgesic in *tubercular laryngitis*, J. L.

[1] Lyon Médicale, 1901, No. 48. [2] British Medical Journal, October 18, 1902.
[3] Münchener med. Wochenschrift, September 9, 1902.

Hatch[1] mentions the remedy as of great value. It lessens the pain in swallowing, and allays the cough. The applications were made either by subcutaneous injection with a Pravaz syringe of about $\frac{1}{6}$ grain into the mucous membrane of the larynx at the seat of the ulcer, or by means of a cotton pledget carrying a known quantity of the dissolved drug. It is asserted that the pain-relieving properties of the remedy used in this way were more marked than with cocaine. The sensation is said to be similar to the benumbing, drying, and thickening feeling of cocaine, but lasts for a number of hours. In some instances the administration of the drug gave rise to sinking spells, prolonged inspiration, with a feeling of apprehension and an irregular, weak pulse. It was thought, however, that these symptoms were largely due to the wretched physical condition of the patient treated.

Hetol. Sodium Cinnamate. This substance, originally introduced into the therapeutics as a remedy of value in treating pulmonary affections (particularly tuberculosis), at the present time finds few champions. With the object of ascertaining its value in tuberculous lesions, Max Wolff[2] directly inoculated the anterior chamber of the eyes of animals, and followed this by treating them with subcutaneous and intravenous injections of hetol. In no instance was he able to determine, either by macroscopic or microscopic study, that the asserted remedy was of any value.

The drug was used in conjunction with sodium sozoiodolate by A. Krokievicz[3] in treating twenty-eight cases of *pulmonary tuberculosis*, all exhibiting pronounced physical signs of the disease and having tubercle bacilli in the sputum. Of the whole number he pronounced two as cured, nine considerably improved, six somewhat improved, while eleven became worse. Injections of 1 c.c. of a 5 per cent. aqueous solution of hetol were made under the skin of the shoulder twice a week, and followed on the second day by $\frac{1}{2}$ c.c. of sodium sozoiodolate. In private practice where injections are impractical he suggests the following formula:

℞.—Sodii cinnamatis	gr. vijss.	vel gr. xv.
Sodii sozoiodolatis	gr. iij.	vel gr. vijss.
Guaiacoli carbonatis	gr. cl.	
Sodii bicarbonatis	gr. lxxx.	
Quininæ hydrochloratis	gr. lxxx.	
Extracti glycyrrhizæ	q. s.	

Misce et ft. pil. No. 200.
Sig.—Two pills three times a day after meals.

[1] American Medicine, October 11, 1902.
Deutsche med. Wochenschrift, July 11
[2] Gaz. lekarski, December 8, 1901.

D. Katzenstein[1] also favors the subcutaneous use of the salt, provided it is used early in the infection. He states that he has frequently observed rapid improvement in the subjective symptoms, such as disappearance of fever and night-sweats, improvement in the cough and expectoration, and an increase in weight.

It will be recalled that two years ago Ewald gave the drug what he considered a thorough trial, and failed to secure the beneficial effects attributed to it by some of its advocates.

Hyoscine. Hyoscine hydrobromate has long been recognized as a valuable nervous sedative, and has been applied with varying success in quieting the tremors of paralysis agitans, for overcoming insomnia, in controlling the jerking in chorea, and to a limited extent in treating alcoholism. The frequent development of unexpected delirium has deterred many physicians from employing the drug, but the recent experiences of some members of the profession that delirium is one of the very common, although entirely harmless actions of full doses of hyoscine, will probably make us less timid in using full doses when occasion requires. Dr. M. K. Lott[2] and Dr. H. A. Hare[3] have recently called attention to the very extraordinary value of hyoscine hydrobromate for curing the *morphine* and *alcohol habits*. By the hypodermic use of very large doses they have been able to secure the immediate withdrawal of the accustomed drug without subjecting the victim to the awful agony which always follows the sudden withdrawal of morphine. It is unnecessary to describe the severe sufferings experienced for days by habitual users of morphine when the remedy is suddenly withdrawn. It is sufficient to state that by the use of full doses of hyoscine given hypodermically this period of suffering may be bridged over until the patient no longer requires or craves his usual drug. The hyoscine is administered in doses of $\frac{1}{200}$ to $\frac{1}{100}$ every thirty to forty minutes until dryness of the mouth, flushing of the face, and mild delirium come on; and after this time continued in doses of $\frac{1}{100}$ or $\frac{1}{200}$ every one or two hours, or in such quantities and with such frequency as to keep the patient continually mildly intoxicated with it, after which time the remedy may be gradually withdrawn. Good nursing and attention to details are, of course, essential to success, but it is stated that patients may be cured of the morphine habit in their own homes by the hyoscine treatment.

Dr. George E. Petty[4] has also secured remarkable results from the use of hyoscine in similar cases, but takes issue with Drs. Hare and Lott as

[1] Münchener med. Wochenschrift, August 19, 1902.
[2] Therapeutic Gazette, February 15, 1902.
[3] Medical News, June 7, 1902.
[4] Ibid., October 18, 1902.

to the quantity of the drug to be administered. He believes the doses advised by these gentlemen are in excess of what is usually required, and that there is no reason for using the remedy in a morphine case for a longer period than from two to four days, so far as the cure of the habit is concerned. He begins treatment by administering calomel, cascara, ipecac, strychnine, and a vapor bath, to be followed upon the succeeding day by castor oil, magnesium citrate, or both, so as to secure free elimination, and thereby prevent the troublesome diarrhœa which usually accompanies the withdrawal of morphine, and also to shorten the period during which it is necessary to give hyoscine.

Petty dwells on the great difference in the susceptibility of different persons to hyoscine, and that full physiological doses and not toxic doses of the alkaloid should be employed.

Iodine and Iodides. Iodine and its compounds are thought by many to be of distinct value in treating *tuberculosis* in its various forms, while others have condemned it as not only useless but harmful. We shall not at this time attempt to harmonize the conflicting views, but call attention to the fact that the advocates of iodine and iodides continue to report favorable results from internal and intravenous injections. An ingenious means of securing the action of nascent iodine in the lungs is claimed to have been discovered by A. Cavazzani.[1]

By injecting potassium iodide into the blood of rabbits, and then causing them to inhale the fumes of oil of turpentine, he claims to be able to bring about the liberation of nascent iodine in the lungs. The discovery is made use of in treating pulmonary tuberculosis. The method has been practised by him in treating both acute and chronic cases for the past ten years, and he claims to have effected some complete cures, and cites cases in which, after six years, there has been no redevelopment of the disease. He states that months, and sometimes a year, are required to effect cures, and that at the beginning of treatment the symptoms become exaggerated.

King's recent paper attributing the curative effect of quinine in malaria to its property of producing a fluorescent light in the blood lends interest to the observation of Regnault,[2] that iodized iodine solution is valuable under certain conditions in treating *malaria*.

He considers quinine by all means our most valuable remedy in treating malaria, and it should be administered before expected paroxysms; but if, in spite of this remedy, the chill appears, tincture of iodine and potassium iodide will cause its prompt disappearance.

The remedy has been used by him with satisfactory results in a

[1] Hospitalstidende (Copenhagen), October 9, 1901.
[2] Revue de Médecine, September 10, 1901.

number of instances. Iodine is not recommended as a substitute for quinine, but in conjunction with it. The remedies should not be combined in the same prescription nor one given immediately after the other, as they are incompatibles.

The formula suggested is as follows:

R.—Tinct. iodi comp.	. . . . .	f℥j.	4 gm.
Potassii iodidi	. . . . .	℥j.	4 gm.
Aquæ	. . . . .	f℥iijss.	100 c.c.

M. Sig.—Teaspoonful at the onset of an attack.

Since the general introduction of ichthyol, the use of iodine in treating *erysipelas* has been almost entirely abandoned; better results, however, may be secured by the use of both of these remedies than with ichthyol alone.

The method suggested by Keirle[1] gives excellent results. The area surrounding the erysipelatous patch is painted with several coats of iodine, a 50 per cent. ointment of ichthyol applied over the patch, covered with gauze, over which a hot compress is applied every four hours. After twelve hours the dressings are removed, the skin washed with warm water, and the application renewed. Usually by this means the disease may be limited and a cure effected in about four or five days. If at any time the inflammation threatens to spread, additional coats of iodine, further away from the original ring, should be applied.

In the treatment of acute *catarrhal* and *follicular amygdalitis* the application of tincture of iodine directly to the inflamed area has been unusually successful in the hands of S. Floersheim.[2]

Being led to apply the tincture with a camel's-hair brush to the tonsils, pharynx, uvula, etc., of a patient suffering with a severe, acute amygdalitis, the beneficial effects were so marked and rapid as to lead him to adopt the method as a routine treatment. In sixty-eight cases treated within the past two years the results have been excellent. The distressing symptoms were, in every case treated, relieved within five minutes after making the application. In cases showing marked improvement and a tendency toward a rapid cure the application was not renewed, but if after twenty-four hours improvement was not satisfactory, the application was renewed. In many cases no other treatment was employed, although in some the usual remedies were used in conjunction with the iodine.

In six cases suppurating or phlegmonous amygdalitis iodine relieved the intense pain, partially reduced the swelling, and seemed to hasten the rupture of the abscess.

[1] Bull. Générale de Thérapeutique, August, 1901.
[2] New York Medical Journal, October 5, 1901.

For a few minutes after the applications of iodine are made within the throat there is usually a good deal of burning pain which, if very severe or persistent, may be relieved by gargling with warm water. If patients experience the burning three or four minutes after the first application, a second application is made.

Our ideas concerning the value of iodides in the treatment of aneurisms, except when of syphilitic origin, have, during the past few years, undergone a decided change, but there is still a deeply rooted opinion that in certain diseased conditions of the bloodvessels, when given over a long period of time, the iodides lower *arterial tension.*

There has long existed considerable difference of opinion as to the effect of iodides upon the circulation of healthy individuals; some writers holding that they were depressant, others, that they were without effect, while some experimenters have stated that iodine and iodide distinctly raise arterial pressure. This subject has recently been studied by Prof. Ralph Stockman,[1] of Glasgow, in conjunction with Mr. Francis J. Charteris. Their clinical experiments were carried out with both sodium and potassium iodides administered by the mouth in doses ranging from 15 to 300 grains daily. Some of the patients had healthy circulatory systems, others suffered from renal or cardiac disease, aneurism, arterio-sclerosis, and bronchitis.

Basch's sphygmomanometer and Gärtner's tonometers were employed to record any circulatory changes which would take place.

Although many patients were brought completely under the influence of the iodides, and one suffered severely from iodism, and felt very depressed and ill, in no case did blood pressure fall or change in the rate or rhythm occur. Their conclusions were that when iodides were given by the mouth, they were entirely without effect upon the circulation of man either in health or with diseased bloodvessels. In addition to their clinical studies of the action of iodide upon the circulation of man, they conducted experiments upon animals by making intravenous injections of sodium and potassium iodides. Sodium iodide injected into the jugular vein produced no fall in blood pressure, and no decrease in the heart's force.

The injection of potassium produced a most decided fall in blood pressure, and diminished the force of the heart beat. These experiments upon animals show the severe depressant effect of the potassium base upon the heart muscle. The authors do not deny the possible value of these remedies in diseases characterized by high arterial tension, but they do not believe in their therapeutic effect based on their direct action upon the heart muscle or arterial walls.

[1] British Medical Journal, November 23, 1901.

Iron Vitellin. This is a reddish powder freely soluble in water, forming a clear, red solution. It is non-irritant, neutral in reaction, odorless and tasteless. The originators of the salt, Barnes and Hille,[1] state that it is a true organic compound of iron, and, unlike the other so-called organic preparations of iron, does not give the blue-black color with hæmatoxylon, which is characteristic of inorganic iron. By experiments upon animals, and by clinical tests, iron vitellin has proven to be readily absorbed and assimilated, and free from any irritating action upon the gastric mucous membrane, and, being non-toxic, there is no limit to the dose.

Lecithin. Lecithin from the yolk of eggs is being used with satisfactory results by many French and German physicians in treating diseased conditions characterized by malnutrition.

In *anæmia* it is said to augment the number of red corpuscles and increase the amount of hæmoglobin. In *neurasthenia* and *wasting diseases* it is said to stimulate the appetite, increase the urea, diminish uric acid, lessen the waste of phosphates, and increase bodily weight. It has also been recommended in *tuberculosis*.

A. Gilbert[2] found tubercular and neurasthenic patients wonderfully benefited by lecithin, administered by the mouth or subcutaneously. When given by the mouth it was usually prescribed in doses of from 1½ to 7½ grains, made into pills, and administered daily. For subcutaneous injections, doses of from 1 to 2 grains were administered every second day.

℞.—Lecithin ovi . . . . . ʒj.
Pulv. althææ . . . . . q. s.
Alcohol . . . . . q. s.

Ft. pilulæ No. xxiv.
Sig.—One to three pills three times a day.

Experiments upon animals and clinical observations upon human beings led Marichaux-Beauchant[3] to conclude that, when administered either by the mouth or subcutaneously, lecithin from eggs increases the appetite, rapidly augments body weight, multiplies the number of red blood corpuscles, and increases the amount of hæmoglobin. According to this author, the substance is a valuable adjuvant to other measures in treating anæmia, cachexia, neurasthenia, and the early stages of tuberculosis. He suggests doses of from 3 to 5 grains by the mouth, or 1 to 2 grains hypodermically.

[1] American Medicine, May 24, 1902.
[2] Therapeutische Monatshefte (Berlin), November, 1901.
[3] Paris Thesis, 1901–1902, No. 110; Gaz. hebd. de Méd. et de Chir., February 2, 1902.

Ariès[1] finds lecithin of very decided value in treating malnutrition of the aged, and particularly beneficial during convalescence from prolonged illness. A study of the urine of a subject under treatment with the remedy showed that the elimination of urea was increased, of uric acid diminished, and that the urine was always rendered markedly acid. Contrary to the findings of most investigators, he states there was an increase in the elimination of the phosphates, at least this was the case in elderly persons.

Magnesium Dioxide. It is claimed by F. Elias, of Berlin, that the new salt of magnesium, which he has been able to produce by chemical processes, is capable when taken internally of giving up to the tissues large quantities of diffusible oxygen. He therefore suggests its use in diseased conditions requiring increased processes of oxidation. Dr. Henry Leffmann made an analysis of the compound and found that its decomposition yielded oxygen in large quantities.

It is possible that clinical experience may prove this new compound to be of value as an oxidizer in the blood or tissues, but it does not follow that, because a chemical is capable by high heat or powerful chemical reagents used to bring about its rapid decomposition, the same reaction will take place in the living body. It will be recalled that some years ago the claim was put forward that, by reason of its power to yield large quantities of oxygen, potassium chlorate would prove a valuable means of furnishing this gas to the blood. It is needless to state how utterly useless it is for such a purpose.

Magnesium dioxide is a white, impalpable powder, without odor or taste, non-irritating, insoluble in water, and said to be non-toxic. In general appearance it is very much like the old well-known laxative, Husband's magnesia. The dose suggested for therapeutic use is 4 to 10 or 20 grains.

Mercury. It has long been recognized as a dangerous procedure to dust calomel into the eyes of persons who are under the influence of iodides. Under such circumstances the calomel is changed into red mercuric iodide, which is highly irritating and leads to severe ulceration. The experiments of F. Lesser[2] demonstrate that, on account of the chemical change, it is unwise to employ calomel either locally, internally, or by hypodermic injection in iodized subjects. The administration of it into stomachs of rabbits under the influence of potassium iodide led to numerous ulcerations of the gastric mucosa, surrounded by a hyperæmic zone, showing the irritating action of the salt. Large crystals of red mercuric iodide were found in the ulcerations and also

[1] Le Mois Therapeutique, 1902, No. 2.
[2] Deutsche med. Wochenschrift, November 28, 1901.

in the stomach contents. The experiments also demonstrated that no ill-results followed the use of medicinal doses of the salicylate, thymol acetate, or bichloride of mercury, or of gray oil in iodized subjects.

The hypodermic use of mercury in severe or obstinate cases of *syphilis* has been extensively employed, but its use by *subarachnoid* injection is an entirely new procedure. Being impressed by the fact that subcutaneous lesions of syphilis improved more rapidly when brought into immediate contact with mercurials, Schachmann[1] conceived the idea of treating severe and obstinate cases of *syphilitic myelitis* by intraspinal injections of benzoate of mercury. He reports four cases, one in detail, treated by subarachnoid injections of 1 c.c. at a dose of a 1 per cent. solution of mercury benzoate. In one case before the injections were begun the patient was unable to stand alone or walk without assistance on both sides. The first injection caused restlessness, insomnia, and slight rise in temperature, which grew progressively less, so that by the time the fifth injection was administered these symptoms had entirely subsided. In the course of twenty-five days, after twenty-three injections had been administered, the patient was able to arise from his bed and walk alone. He slept soundly, had no pain, and his general condition seemed much improved. It is stated by Schachmann that, although the girdle pains and other syphilitic manifestations in this case had been relieved by the use of subcutaneous injections of mercury, they had been without effect upon the myelitis.

Methylene Blue. Methylene blue has proved of distinct value for internal administration, and also as a local application in a number of diseased conditions; and as it is sometimes confused with "methyl blue," an entirely different substance, it is important that physicians should be on the alert to detect the substitution of one drug for the other.

A very simple test will enable anyone to readily distinguish between the two substances. By the addition of a small quantity of water of ammonia to a weak solution of methylene blue it is decolorized, while no decolorization follows in solution of methyl blue.

There are two kinds of methylene blue upon the market, the medicinal and the commercial. The medicinal is quite pure, while the latter is frequently contaminated by salts of zinc and arsenic, and is unfit for medicinal use. The only sure plan for prescribers is to insist that the compounder shall secure his supply from a reliable manufacturer.

The remedy has been extensively employed internally in treating *acute specific urethritis, malaria, neuralgia,* and lately has been suggested as a *nervous sedative.*

[1] Bulletin de la Société Médicale des Hôpitaux de Paris, October 24, 1901.

Gynecologists, rhinologists, and laryngologists have testified to its anti-inflammatory and sedative action when locally applied.

T. H. Van de Velde[1] called attention to the tendency of the drug, even when quite pure, to at times give rise to irritation of the stomach, bowels, kidneys, and bladder, as evidenced by vomiting, diarrhœa, scanty urine, and strangury. In addition to these disagreeable effects the drug sometimes gives rise to vertigo, and when administered hypodermically produces considerable pain, which often lasts a number of hours.

Abscesses are very likely to follow hypodermic injections of it, unless the precaution is taken to boil solutions intended for subcutaneous use.

The probable value of methylene blue as a nervous sedative seems to have been first suggested by Ehrlich and Guttman, and Bodoni observed such properties while using it internally in testing the activity of the renal functions. It was later tried by him upon fourteen cases of different forms of *mania*, and was found to act satisfactorily. More recently Drs. D. E. Hughes and Elizabeth Lovelace[2] tested the sedative action of the drug upon twenty-two cases in the insane and detention wards of the Philadelphia Hospital. While their results were not so uniformly good as those of Bodini, they were sufficiently marked in particular cases to lead to the hope that further study and trials would establish its value as a sedative.

A review of the cases reported shows that all were severe outbreaks of different forms of mania, and were in a state of wild excitement when methylene blue was begun. The quieting effect seemed to be different from that produced by hypnotics or narcotics, for there was no dulness or hebetude following its use; patients usually simply ceased to be excited and became normally quieted. Patients slept well at night, and the drug did not induce sleep during the day. The beneficial influence of the drug usually came on three or four hours after its administration, and lasted from fifteen to twenty-four hours. The remedy seemed to act with somewhat greater promptness when given hypodermically, but was also effective when given by the mouth. In hypodermic doses of 1 grain, once or twice a day, indurations and abscesses at the seat of puncture were at first of frequent occurrence; but later, when it was learned that thorough sterilization could only be secured by boiling the bottle containing the solution, no abscesses occurred. When given by the mouth it was usual to administer 2 grains in capsules, night and morning.

After securing continuous calmative effects for several days, the doses

[1] Centralblatt f. Gynäk., 1902, No. 23.
[2] Philadelphia Medical Journal, March 22, 1902.

were either given at longer intervals or discontinued altogether; but in one case the remedy was given hypodermically for fourteen consecutive days, and in other cases by the mouth for fifteen, twenty-one, thirty-nine, and forty-two days without any ill-effects. In only one case was there mild depression after the use of the drug, and one other developed vertigo. Patients were said to be particularly free from gastro-intestinal disturbances.

Of one hundred cases of *malaria*, treated by A. De Blasi[1] with methylene blue, he claims sixty-two were completely cured by its use. The remedy was thought to be effective only when the parasites have been circulating in the blood some time. He warns against the administration of the blue to women during their last two months of pregnancy, as he has observed painful uterine contraction, which is liable to induce miscarriages in such patients. As a local application in the treatment of *ozæna* the chemical has received the approval of a number of writers. Beth, Bonnet, and Hallopeau secured good results in syphilitic cases by irrigating the nares with a 2½ per cent. solution. It was usually necessary at the beginning to irrigate the nares three times a day, and gradually to lessen the application to once a day. The irrigations must be continued for two or three weeks. The usefulness of the remedy was limited to the secondary infection, causing a rapid disappearance of the fetid odor. It unfortunately discolors the lips and nares.

Observing that methylene blue was a good stain for the spindle-shaped bacilli and spirillæ found in the throats of persons suffering with *ulcero-membranous stomatitis*, A. Siredey[2] made use of the chemically pure substance in powdered form, as a local application in a case of staphylopalatino stomatitis, and was highly pleased by the rapidity of the cure. The powder was applied by means of a cotton swab, followed by gargles of boric acid, and after eight days, during which time six applications had been made, cure of the stomatitis was complete.

Nitroglycerin. Observing in the current medical literature that nitroglycerin is occasionally recommended as a stimulant in treating surgical shock, collapse, and allied states, we fear that it is looked upon by some as a heart stimulant, and is sometimes applied without a very clear understanding of its action upon the circulation.

The drug is not a stimulant to the heart, but, by reason of its prompt and powerful action in dilating the arterial vessels, is of the very greatest value in treating circulatory conditions characterized by heightened arterial tension due to narrowing of these blood paths. It is true that

[1] Gazetta degli Ospedali, March 23, 1902.

[2] Bulletin de la Soc. Méd. des Hôp. de Paris, November 14, 1901, and La Presse Médicale, March 1, 1902.

when the heart is laboring and slowed in its efforts to pump blood into contracted arteries and arterioles, nitroglycerin and other nitrites will increase its rate, and improve the circulatory condition. This improvement is not brought about, however, by stimulating the heart muscle, but by dilating the arterial bloodvessels, thereby permitting the heart to do its work with less effort. The increase in rate is also due, in part, to the depressing effect upon the pneumogastric nerves, thereby lessening their inhibitory influence upon the heart. We can readily understand how a whiff of amyl nitrite, which is very fleeting in its action, might, by its influence upon the pneumogastric nerve, be of value if the heart has almost stopped, but the other nitrites which are more lasting in their effects are not suitable for administration in shock or collapse, conditions in which the blood paths are already relaxed and dilated.

Nitroglycerin has become the most popular nitrite, and is extensively employed in treating *arteriofibrosis*, *interstitial nephritis* with heightened arterial pressure, *chronic parenchymatous nephritis*, and also as an antispasmodic in *asthma*, vomiting, renal and hepatic colics. Amyl nitrite has a more rapid but fleeting effect than nitroglycerin, while cobaltonitrite of potassium, potassium nitrite, and sodium nitrite are all less rapid, but more prolonged in their effects.

In certain chronic affections where nitrites are being administered it becomes necessary to continually increase the size of the doses, as patients rapidly become accustomed to the drug. The possible reason for this is that, as nitroglycerin gradually replaces the natural physiological vasomotor depressant secreted by the thyroid gland, the cells concerned in the elaboration of this secretion atrophy from non-use, and finally cease to supply the special principle concerned in vasomotor relaxation.

The bloodvessels of the brain, while not under the control of the vasomotor centres in the medulla, may be indirectly influenced by drugs acting upon the general vascular system. Dr. Alfred Gordon[1] reports two cases of venous engorgement with arterial ischæmia of the brain, in which strikingly beneficial effects followed the use of nitroglycerin. Both were cases in which arterial tension was abnormally high, one had atheromatous arteries, and both suffered from occasional attacks of vasomotor ataxia.

The good effects were brought about by increasing the supply of arterial blood at the expense of the venous engorgement.

Physicians also seem to lose sight of the fact that spirit of nitrous ether is a nitrite, and that its therapy is based upon its vasomotor effect. In the presence of acute fevers with high arterial tension, it

[1] Therapeutic Monthly, December, 1901.

relaxes the bloodvessels, permits the blood to flow through dilated peripheral vessels, where it rapidly radiates its heat. The diuretic effect of this drug is also produced in a similar manner to all other nitrites, that is, by the dilatation of the renal bloodvessels.

Orthoform. Insufflation of orthoform for the purpose of relieving painful deglutition is extensively practised, but this mode of treatment necessitates a visit by the patient to the office of his physician. Dr. S. S. Cohen[1] states that for the past two years he has been making use of lozenges, each containing from ⅛ to 1 grain of orthoform, for temporarily relieving the pain in cases of acute and subacute *sore-throat*, whether of rheumatic or other origin, and in cases in which pain in swallowing has been caused by ulcerative or infiltrative conditions, involving the epiglottis and arytenoid eminences. Bouveron and Siraud[2] have found that the internal administration of from 7 to 15 grains of orthoform, taken three or four times a day, may be employed with success against the essential headache of *syphilis*. When the headache is intermittent, the powder should be taken about two hours before the expected time for the pain to appear, and again during the latter part of the night. Should the ingestion of this drug provoke the sensation of heat or irritation of the stomach, an equal quantity of bicarbonate of sodium may be taken with each powder, to correct this disagreeable feature.

Phosphorus. The administration of phosphorus in cod-liver oil finds favor with many physicians. If such solutions are permitted to stand the phosphorus slowly decomposes. Dieterich states that if the oil is first supersaturated with carbonic acid gas the phosphorus does not undergo oxidation; and, furthermore, that carbonization preserves the oil and prevents it from becoming rancid. As it is a common practice to prescribe phosphorus combined with strychnine, quinine, nitroglycerin, or zinc valerianate in pill form, and as there was no definite knowledge as to whether such a combination decomposed either the phosphorus or the other ingredients, W. H. Martindale[3] made a complete chemical analysis of such pills. The chemical changes or interaction between the drugs—in pills which had been made for several weeks and properly protected by coating—was so slight as to be of no consequence, except possibly in those containing zinc valerianate. In the analysis of these zinc phosphate was found, but it may have been developed during the processes of analysis. Conflicting views regarding the therapeutic value of phosphorus are constantly observed in the current medical literature. The demonstration by Wegner in 1872,

[1] American Medicine, November 9, 1901, p. 751.
[2] La Semaine Médicale, December 4, 1901.
[3] British Medical Journal, March 8, 1902.

showing that when administered in repeated small doses to animals phosphorus stimulates bone growth, seemed to place the remedy upon a firm scientific basis for use in treating cases of deficient bone growth. Since that time many clinicians have testified to the value of the drug in treating *rickets*, while others have failed to secure satisfactory results from its use. As the new tissue formed by phosphorus is at first gelatinous, and remains so if the food is deprived of lime, it is probable that disappointing results in some cases may have been owing to the failure to supply lime while administering phosphorus. The official preparations of phosphorus, for which formulæ are given in the pharmacopœia, are phosphorated oil containing about $\frac{1}{100}$ grain of phosphorus to each minim, the elixir of phosphorus containing about $\frac{1}{64}$ grain of phosphorus in each teaspoonful, and the pills, each containing $\frac{1}{100}$ grain of phosphorus. Both of the liquid preparations undergo oxidation, and should be freshly prepared when required. The pills are coated with tolu, and keep well.

Quinine. ACTION ON MALARIAL PARASITES. Much of interest on the subject of quinine has been under discussion the past year. The inquiring mind has not been satisfied with the knowledge that the drug is a specific in malaria, but seeks to learn the nature of its action upon malarial organisms, the most satisfactory methods and doses for administration under peculiar circumstances, and also more about the untoward effects of the alkaloid. The effect *in vitro* of quinine solution of various strengths upon malarial blood has been the subject of exhaustive study by Dr. L. Monaco and L. Panichi,[1] and they have reached some interesting conclusions. They announce that a drop of weak quinine solution added to a fresh specimen of malarial blood causes excitement, temporary contraction, and emission of pseudopodia, and a somewhat stronger solution increases the excitement and terminates in the escape of the parasite from the blood corpuscle; while a still more concentrated solution of quinine permanently shrivels the parasite and causes its retention in the corpuscle. In practice they attempted to use quinine in such quantities as to cause the detachment of the plasmodia from the blood corpuscle. The smallest forms of parasites were found to be more resistant to quinine, and that all plasmodia grow more resistant to the drug the longer the interval since the febrile attack. It is their belief that at the time of a malarial paroxysm there is a substance in the blood which has an antiparasitic action, and that quinine administered at such a time is reinforced by this substance already in the blood. The only form of malarial organism they believe to be unaffected by this antiparasitic substance is the young unpig-

[1] Riforma Medica, January 2 and 3, 1902.

mented variety found in the æstivo-tertian type. Upon the other hand, pigmented forms are resistant to quinine during apyrexia, but become less so during the febrile attack, at which time they may be detached from the red blood corpuscle with a comparatively weak solution of quinine. By reason of the absence of the antiparasitic substance in the blood or from the presence in it of some—as yet unknown—antagonistic substance, the pigmented and non-pigmented parasites display great resistance to quinine during pernicious malaria. In recent articles, A. F. A. King[1] presents a number of facts to prove that the curative action of quinine in malaria may be brought about by its power to kill the parasite with *fluorescent light.* It is maintained that malarial organism will not sporulate in the dark, and that the light it obtained in the blood was necessarily red. He assumed that the malarial amœba, like amœba proteus, streams in red light, but not in violet; hence, the curative action of quinine might be due to its fluorescence producing violet rays of light in the blood. The facts set forth to corroborate this theory are that esculine and fraxine, both of which produce fluorescence, are effective remedies in malaria. He quotes Henry Bence Jones as having demonstrated that an efflorescent substance normally exists in the blood of animals and man, and Edward Rhoads and William Pepper as having demonstrated thirty years ago that in the blood of malarial patients this efflorescent substance fell below the normal, and, furthermore, that this substance could be increased in the blood by the administration of quinine. He explains the failure of the alkaloid to cure certain forms of malaria (in which paroxysms do not occur, but in which the infection is usually associated with marked cachexia) by stating that these parasites are not generally found in the peripheral circulation, where they can get light, but in the darker recesses of the body, such as the spleen, liver, bone marrow, and brain, where the fluorescent property of quinine is impotent. He accounts for the regularity of malarial paroxysms by the arrest in the capillaries of the skin of swollen blood corpuscles containing malarial parasites, which, after exposure to sunlight sporulate and give rise to the chill; followed by fever in which the capillaries are markedly dilated, and this is followed by the sweating stage, with contraction of the skin capillaries within which are entrapped the parasites, which are again exposed to sunlight, with a repetition of the paroxysm. It is his belief that such organisms exposed to the fluorescent violet light of quinine are killed, and the infection thereby terminated.

In a paper read before the section of General Medicine at the College of Physicians of Philadelphia, December 9, 1901, Dr. David

[1] American Journal of the Medical Sciences, February and June, 1902.

Riesman spoke of the malarial paroxysms and their curability with quinine. It has long been recognized that quinine to be of value in malaria must be used in heroic doses. The usual method for preparing the alkaloid for hypodermic injection is to increase its solubility by the addition of small quantities of an acid. As is well known, such injections are quite painful, and are often followed by sloughing or abscesses. The method suggested by James W. Gray, Jr.,[1] appears to be decidedly preferable to that usually followed. This method consists in the use by hypodermoclysis of a ½ of 1 per cent. solution of quinine hydrochlorate in warm normal salt solution. By this means, in addition to securing the introduction of about 25 grains of quinine in each pint administered, we also secure the beneficial eliminative effect of the saline solution. The injection must, of course, be given with the strictest antiseptic precautions. In cases of great urgency the injection may be made directly into a vein. Some cases of obstinate malaria do not readily yield to quinine administered by the mouth, and in such cases, during the past year, many writers have testified to the value of the hypodermic use of the drug.

We find clinicians dividing themselves into three classes regarding the use of quinine in the treatment of so-called *hæmoglobinuria*. Some strongly maintain that as the disease is caused by malarial organisms, its cure lies in the administration of full doses of quinine. Others believe that the alkaloid is the chief causative factor, and should never be administered in the presence of hæmoglobinuria. Still another class hold that hæmoglobinuria may be caused by either malarial parasites or quinine, and they direct their treatment accordingly. William Britt Burns[2] does not believe that quinine is ever the sole factor in the production of hæmoglobinuria, and he does not hesitate to use the drug in the presence of the disease. W. Shropshire[3] favors the administration of quinine hypodermically in full doses. He reports two cases in which this treatment was thoroughly tried. In two severe cases of malaria, in which small doses of quinine were given, the patients developed hæmoglobinuria, which promptly disappeared after they were thoroughly cinchonized by 20 grains of quinine administered hypodermically every five hours. He doubts the effects of quinine in producing hæmoglobinuria. I. Pailloz[4] reports six cases of malarial hæmoglobinuria treated with quinine, and regards with favor the repeated hypodermic injections of 30 grains of quinine as indicated. He believes the disease is due to malarial organisms and not to quinine,

[1] Memphis Medical Monthly, December, 1901.
[2] Ibid., September, 1902.
[3] Georgia Journal of Medicine and Surgery, September, 1901.
[4] Archives de Médecine et de Pharmacie militaire, September, 1901.

and that the absence of hæmatozoa and pigment from the blood does not prove that bilious hæmoglobinuria is not malarial in origin. It is his experience that hæmoglobinuria appears after the chill. O. Lerch[1] states that the æstivo-autumnal parasite is always at fault, but that climate and certain individual predispositions are also active causes in setting up the hæmoglobinuria. It is his opinion that several varieties of hæmoglobinuria must be considered. In some cases the attack will appear with the sporulation of the parasite, which may be found in the blood, and is best treated by the hypodermic use of quinine. Another variety of the disease is post-malarial, in which all parasites have disappeared from the blood; and still another in which quinine seems to have been the cause. The last two varieties he believes are to be treated with rest, fresh air, eliminants, and supportive treatment. He holds that a fever which does not yield to proper administration of quinine in a few days is not due to a plasmodia; but is post-malarial, toxic, or inflammatory, or both, and further use of quinine is injurious. M. Otto[2] reports a case in which the patient contracted and developed malaria of a quartan type in a Northern climate, and after about four weeks developed hæmoglobinuria. The disease was influenced by moderate doses of quinine during four weeks' treatment, but at the end of the fifth week, an hour and a half after taking 7½ grains of quinine (with the object of aborting the expected chill), hæmoglobinuria developed. The remedy was continued in moderate doses daily, without either apparent harmful or beneficial effects, until finally, about five weeks later, after a dose of 15 grains, hæmoglobinuria again appeared. The quinine was continued in moderate doses until the patient finally recovered. It was the opinion of Otto that quinine was the exciting cause of hæmoglobinuria. Dr. Joseph C. Curry[3] reports two cases of hæmoglobinuria, one of which died under quinine treatment, and the other dying without the treatment. He considers the drug harmful in the treatment of this condition.

Idiosyncrasies to quinine are frequently manifested by the appearance of rashes, which may be of almost any character, but usually appear as urticaria, roseola, erythema, purpura, bullæ, or scarlatiniform eruption. Workmen engaged in the manufacture of quinine are said to show eczematous eruption. The rash is frequently accompanied by itching and affections of the mucous membranes, and followed by desquamation. This is well illustrated in the cases collected from the literature and reported by H. C. Wood, Jr.[4] In the presence of fever, constitutional

[1] New Orleans Medical and Surgical Journal, November, 1901.
[2] Deutsche med. Wochenschrift, January 23, 1902.
[3] Journal of American Medical Association, May 3, 1902.
[4] Therapeutic Gazette, January 15, 1902.

symptoms, irritation of the mucous membranes, and scarlatinoid rash, with desquamation, after quinine, the case may so closely simulate scarlet fever as to make the diagnosis difficult. The diagnosis may ordinarily be made by a knowledge of the idiosyncrasy to quinine or by giving another dose of the alkaloid after the symptoms have disappeared. In scarlet fever the rash usually first appears upon the flexor surfaces, and albumin is almost invariably found in the urine. Persons having once shown an idiosyncrasy to the drug, as a rule, are always similarly affected, even by the smallest dose. In a case of his own, reported by Wood, the patient, a woman, after taking two teaspoonfuls of compound tincture of cinchona shortly developed a well-marked eruption over the extensor and flexor surfaces of the forearm. A case reported by Stelwagon[1] well illustrates the susceptibility of some persons to quinine. The patient, a man, had at various times suffered with not less than twenty attacks of scarlatiniform erythema, followed by desquamation (with more or less itching), lasting several weeks, caused by taking cinchona preparations. In one instance the eruption followed a dose of compound elixir of cinchona, another after taking a sip of bitter wine of iron, again after taking compound syrup of hypophosphites. On another occasion the eruption was caused by taking rhinitis tablets containing $\frac{1}{16}$ grain of quinine. Care must be taken not to attribute all rashes appearing while treating malarial patients with quinine to the drug, as the disease itself may originate skin lesions of various characters. Martin F. Engman[2] calls attention to the frequency of skin eruptions associated with malarial infection. His conclusions, after studying eighteen such cases, are: "1. It is highly probable that certain affections of the skin, as pruritus, urticaria, angioneurotic œdema, erythema, pompholyx, zoster, eczematoid eruption, and gangrene, may be due to malarial poisoning. 2. In such cases there is generally a periodicity in the intensity of the eruption symptom. 3. There may be marked or slight constitutional disturbances, or eruption may occur without any other symptoms of paludism. 4. Nephritis may complicate the picture in severe cases and seem to be the apparent cause of the dermal manifestations, whereas the malarial infection is the sole etiological factor. 5. When an eruption is associated with malarial infection it quickly recovers under specific treatment."

Radiotherapy. The recent literature bearing upon the therapy of the X-rays, and especially its application in the treatment of malignant growths, has become so voluminous, that it is only possible to call atten-

[1] Journal of Cutaneous and Genito-Urinary Diseases, January, 1902.
[2] Medical Bulletin of Washington University, St. Louis, January, 1902.

tion in this article to some of the more important writings upon the subject.

All active therapeutic agents capable of great good if used recklessly or unintelligently may be productive of harmful results, and there is no exception to this rule in the use of this comparatively new agent. In the journals, during the past few years, there have been numerous reports of accidents occurring from the use of the rays for diagnostic, therapeutic, or other purposes.

The character of the injuries varies from cases of mild or persistent dermatitis to burns of the first, second, and third degree. An analysis of these cases by E. A. Codman[1] shows that the number is not so great as it appears, and considering the very great number of exposures, the percentage of accidents is extremely low. The frequent republication of each case keeps the matter constantly before the readers of medical journals.

He furthermore shows that many of the reported cases (a total of less than 200) occurred several years ago, before there was any general knowledge that such accidents were possible, and when long and close exposures were much more common than at present. With knowledge gained of experience, and with greater perfection of apparatus and technique, he believes that there should not be more than one accident in ten thousand exposures.

That burns may and do sometimes follow the use of the rays by a careful, experienced, and expert operator, is an undeniable fact, and if patients are informed of this fact and accept the risk, it will relieve the physician of any annoyance of a suit for damages.

Burns have occurred from using both static and coil machines, from hard and soft tubes, from tubes with short and long sparks, from long and short exposures, and from close and distant applications. There seems to be a tendency among writers to consider the rays applied from a static machine less liable to produce burns than from a coil machine, especially if the tube is hard and gives a short spark.

Low voltage and low ampèrage from the secondary coil are also said to be less likely to burn than when high, but such an apparatus is not always most active therapeutically, and each operator appears to have his own ideas as to the arrangement of his machine, etc. Some believe the soft tube more energetic for operating upon superficial tissues, and the hard tube for deeper structures. The most important point, however, to be taken into consideration in avoiding burns seems to be the length of time of exposure and the distance at which the tube is to be held from the surface of the body.

[1] Philadelphia Medical Journal, March 8 and 15, 1902.

Codman suggests that for therapeutic purposes an exposure of six inches may in most instances be considered within the range of safety. In addition to the chief factors, the apparatus, spark length and voltage, primary current, quality of tube, distance and time of exposure in avoiding burns, the idiosyncrasy of the patient must be taken into consideration; some individuals are endowed with tissues very susceptible to the influence of the rays, while some appear to be but slightly affected by them. Of course, the surrounding tissues of a part not intended to be acted upon should be protected from the rays when a part of its structure is being operated upon. The burns of the X-rays are peculiar in the fact that the evidence of injury in many instances is delayed for days or weeks; therefore, it is a safe procedure to delay operations for several days at least after the first application.

The burns, while differing pathologically from those received from thermal agents, are treated in a like manner. Carl Beck,[1] in an article upon the treatment of carcinoma by the X-rays, states that between the burns and the changes produced by these rays there is a characteristic difference, in as much as the latter are noticed only after about two weeks. He begins with an exposure of five minutes, and increases the time to ten minutes after six or seven days. If the patient does not show any harmful effects after the second week the exposures are made more frequently, one every day, until intense inflammation takes place. At the beginning his tube is placed at a distance of about four inches, and if no idiosyncrasy is shown, the distance of the tube is lessened to one inch. A microscopic examination of the X-ray burns revealed a disturbance in the wall of the bloodvessels. The nutrition of the cells is impaired by the influence of the X-rays. After prolonged exposure, a hair, for instance, loses its structure; there is no root visible, and it terminates in a point. The narrowing of the lumen of the bloodvessel is brought about by a thickening of its tunica intima, and fibrous tissue is deposited in reticular order.

The same changes take place in the tunica muscularis and adventitia.

In neoplasms the changes brought about resemble a chronic inflammation, and if the exposure has been too long, a necrosis of the tissues takes place. Although the surrounding parts should be carefully protected, no shield should be used directly over the tumor subjected to treatment, as all the influence of the Röntgen light is desired.

Between the exposures Beck uses the following salve:

℞.—Xeroformi . . . . . 1 gm.
Adeps lanæ hydrosi . . . . . 10 gm.

Aside from its use for diagnostic purposes, the X-rays are being extensively employed in the treatment of *sarcomata, carcinomata, lupus,*

[1] Medical Review of Reviews, August 25, 1902.

rodent ulcers, acne, Hodgkin's disease, and as a depilatory. Among the first to use the rays in treating epitheliomata were Johnson and Merrill, who published their results in the *Philadelphia Medical Journal* of December 8, 1900. Their report was closely followed by those of Sequeira, of London; Steinback, of Stockholm; Williams, of Boston; Andrew Clarkes, of London, and George G. Hopkins, of Brooklyn.

During the past year the reports of many reliable writers and exhibition of cases greatly improved, or apparently cured, leave little doubt as to the remarkable effects which may be secured. The specialists in this line of work are modest in their claims, and they freely admit that the apparently cured cases have not as yet been from under treatment long enough to justify the assertion that there will be no return of the growths. The results are placed on record, and final decision must come later, but enough has already been accomplished to make it positive that the measure should be employed in all inoperable cases when operation is refused, and as an adjunct to surgical measures in many others. It has been my good fortune to see what appears at this time to be some very remarkable cures of cases of epitheliomata and lupus which were treated in Philadelphia by Dr. W. M. Sweet.

The definite limitations of surgical measures in many of these cases are well understood, and the X-rays, while not recommended as a substitute for the knife, have undoubtedly been employed with great benefit as an adjuvant in cases of recurrent malignant growths, and also in many inoperable ones. Not only are ulcerating surfaces frequently healed, glandular enlargements reduced, and pain in a great majority quickly and more permanently relieved than with opiates, but the neoplasms, in many cases, entirely disappear.

The value of radiotherapy in treating morbid growths is well illustrated and described by W. A. Pusey[1] in a concise paper detailing the treatment and results secured in four cases of tuberculosis of the skin, eight of epitheliomata, six of carcinomata of the breast, six of deep-seated carcinomata of the neck and head, five of carcinomata of the abdominal cavities, three of sarcomata, one of granuloma of uncertain origin, one of keloid, two of pseudoleukæmia, and one of splenic leukæmia.

This array of thirty-six cases is not one of unbroken successes, but they bring forcibly to our minds how much may be accomplished in some cases by means of the intelligent use of the X-rays. Pusey distinctly states that the method of treatment is not advised as a substitute for operations in operable cases of maliguant growths, but should be a reserve method of treatment. He suggests its use in all cases of

[1] Journal of American Medical Association, April 12, 1902.

malignant disease as a prophylactic measure subsequent to operation; in all inoperable cases it should be tried, as in all such cases there is a probability of its relieving pain, and a possibility of inhibiting the progress of the disease.

The advantages claimed for the method are that it is painless, it destroys diseased tissues, leaving healthy tissues with small scars in its place, its availability in many inoperable cases about the nose, orbit, etc., and its pain-relieving properties.

All of the cases treated were unsuitable for surgical operations. The greatest successes were attained in the cases of lupus and epitheliomata, all of which were apparently cured.

Three cases of recurrent carcinomata of the breast are apparently well, while two severe inoperable cases under treatment for four and five weeks were without benefit; another of the same kind in which there were sixty-six treatments during five months, must be classed as a failure.

In his six cases of carcinomata of the head, in which the oral cavity or orbit was involved, the most that can be said for the treatment was that the pain was relieved in some, and in most of them the growth of the tumors was for a time retarded. All ultimately died.

There seems to have been practically no effect from the use of the treatment in cases of carcinoma in the abdominal cavity. The applications were made in five reported cases. Of the three cases of sarcomata, one involving the tissue of the neck was markedly benefited and for a time apparently cured, but, upon discontinuance of treatment after a few months, symptoms of recurrence were observed.

A case of osteosarcoma of the shoulder and another of sarcoma involving the pectoral muscle and shoulder were considerably relieved of pain, but not otherwise improved.

The cases of granuloma and keloid were cured.

In the two cases of pseudoleukæmia under treatment the glandular enlargements, although formerly very pronounced, have almost entirely disappeared, pain was entirely relieved, and the general physical condition of both patients markedly improved. No apparent relief followed the use of the X-rays in the only case of splenic leukæmia treated.

In no diseased condition have the rays been of greater benefit than in tuberculosis of the skin.

Freund[1] is of the opinion that in lupus the same beneficial results may be secured from the use of X-rays as from Finsen's apparatus, the time for effecting a cure and the resulting scar being about the same. He has also secured favorable results in cases of *ringworm of*

[1] British Medical Journal, September, 1902, p. 339.

the scalp, tinea favosa, sycosis and *hypertrichosis*, in all of which the chief therapeutic feature is the removal of the hair.

G. H. Lancashire[1] is favorable to radiotherapy in similar diseases. In cases of extensive lupus vulgaris affecting the face he prefers the Roentgen rays to treatment by Finsen's method. The application of X-rays also proved valuable in cases of lupus affecting mucous membranes. He has seen only one case of rodent ulcer which showed no response to radiotherapy.

Although skeptical when he first began the use of X-rays for malignant growths, W. L. Heeves[2] soon became convinced of their value. He gives the clinical histories of cases of painful tubercular arthritis and of varicose and tuberculous ulcers which were rapidly cured, and praises the prompt pain-relieving properties of the rays.

Four cases of epitheliomata (microscopic study not made) are reported, with illustrations, by G. E. Pfahler.[3] In one the growth involved the entire base of the nose and extended into the inner canthus of each eye.

Treatment was applied by covering the whole face, except the growth, with a lead mask, and applying the light for ten minutes at a distance of 25 centimetres upon alternate days. The apparatus used at first was a current strength of 10 ampères, a soft light from a vacuum corresponding to a parallel spark gap of about 4 to 6 centimetres. The patient rapidly improved during three months' treatment, but by reason of the redevelopment of violent symptoms of insanity it was necessary to interrupt the treatment for about three months, when it was resumed, the exposure being longer and the tube at a shorter distance from the growth. A dermatitis caused a discontinuance of the treatment, but at the time of the report healing had been almost complete.

Another was a man, aged fifty-five years, who was suffering from general paresis and an epithelioma involving the inner canthus of the left eye, both lids, and the nose. Subjected to the same treatment, improvement in the growth was marked and rapid. After about four months, when the cure was thought to be almost complete, the patient died of paresis.

The third case was also one of epithelioma about the orbit, which was completely healed after nineteen exposures, during one and a half months.

The fourth case was one of epithelioma upon the right side of the nose and involving the canthus of the eye in a woman, aged seventy years. This case was treated every day for five days, then interrupted

[1] British Medical Journal, May 31, 1902.
[2] Therapeutic Gazette, October 15, 1902.
[3] Ibid., March 15, 1902.

for five days. After that time exposures were made at longer intervals, the longest being ten days. After sixteen treatments during two months the growth had entirely disappeared, and the patient was apparently cured. In this case there was a rather severe burn of the ear and upper part of the chest and shoulders, which had not been fully protected.

One of the most enthusiastic writers in regard to the value of the X-rays for morbid growths is Dr. William J. Morton,[1] who states that by its use the cure of superficial epitheliomata is established, and its beneficial or probable curative influence in sarcomata or carcinomata extremely promising.

In addition to the statement that a certain number of malignant growths have been cured, the rays relieve pain, reduce the size of the growths, bring about a cessation of discharges, and remove foul odor if present. They also soften and cause the disappearance of lymphatic nodes and also lymphatic enlargements not distinctly submitted to treatment, but often quite distant from the growth. There is usually improvement in the general health of the individual treated.

X-radiation is recommended prior to surgical operations to clear the tissues of cancer particles and foci, and to circumscribe the disease, and after operations to preclude a recurrence.

For superficial use he makes use of a medium soft tube, but for treating internal growths a hard one is recommended. As do all writers, he advises against the use of this powerful agent by the inexperienced.

G. F. McCaw[2] reports a primary epithelioma of the uvula and soft palate with recovery in a woman, aged thirty-seven years. The treatment first instituted was excision of the tumor, and then the patient was subjected to the X-rays for twenty minutes—at first three times a week, later only once weekly.

Rudis Vicinsky[3] is also impressed with the value of radiotherapy for treating superficial cancers and as a prophylactic before and after surgical operations in cases of carcinoma of the breast.

E. A. Peters[4] treated, with much benefit, a case of recurrent, slow-growing celled carcinoma of the breast with the rays. During about a month's time and after ten applications the growth gave every promise of healing, when the patient, a woman, aged ninety-seven years, suddenly died of croupous pneumonia. Relief from pain in the tumor and subsidence of glandular swelling were noticed from the beginning.

[1] Medical Record, March 8 and May 24, 1902.
[2] New York Medical Journal, August, 9, 1902.
[3] New York Medical Record, August 30, 1902.
[4] British Medical Journal, March 1, 1902.

Dr. George G. Hopkins,[1] who was among the first to employ the rays as a therapeutic measure, continues its use, and his experience of three and one-half years convinced him of the certainty of action of the agent to absolutely control the growth of many cases of carcinomatous and other malignant and benign tumors. The effect of fluorescent rays, he says, in inoperable cancer is simply wonderful. His most satisfactory results have been in applying the treatment in recurrent carcinomata of the breast after amputation. Until recently he refused to apply the rays in cases of uterine cancer, but he is now treating many such inoperable cases with a considerable degree of success. In the hemorrhagic form of cancer of the uterine neck and vaginal wall, the Finsen light is employed in conjunction with the Roentgen rays, and he states that his success has been gratifying.

The treatment has also been employed with gratifying success in cancer of the tongue, larynx, trachea, and œsophagus. Hopkins believes that malignant growths of deep structures are amenable to treatment with the rays; carcinoma of the stomach being brought within their curative influence. He prefers the static machine, and uses the soft light in treating external growths and the hard tube for treating deeply-situated tumors.

Johnson and Merrill report[2] the results obtained in twenty-seven cases of carcinoma, lupus, etc., treated by the X-rays, and of sixteen cases of epithelioma, ten were apparently cured, four remained stationary, and only two cases failed as to retrocession, although the pain was stopped and the discharge decreased. Seven were inoperable cases of carcinoma, and in not one of these improvement could be obtained beyond the alleviation of the pain. Good results were noticed in a case of lupus vulgaris, but in two patients having fibroma no changes could be obtained.

They subjected the patients to strong exposures, as it is their belief that the quicker the reaction of the skin is produced the sooner further treatment has to be stopped.

They are of the opinion that the X-ray has a selective action on the diseased skin.

While fully aware that the time has not yet arrived when very definite conclusions can be reached regarding the permanent value of X-ray treatment in sarcomata, Dr. William B. Coley, who has been much interested in the study and treatment of these growths, is of the opinion that the results in the cases thus far reported prove that Roentgen rays have a remarkable inhibiting action upon them, and in

[1] Philadelphia Medical Journal, April 5, 1902.
[2] American Medicine, August 9, 1902.

many cases of even far advanced and inoperable malignant growths the rays may cause a total disappearance of the tumor, often without breaking down the tissue.

In the *Medical News* of September 20, 1902, he reports ten inoperable cases of sarcomata under his personal observation, some of which were treated with X-rays and some with Coley's fluid plus the rays. Of these, three appear to be failures, two were apparently cured, one is still under treatment and is improving; in one the tumor is much improved, but is developing signs pointing to metastases in the lungs, in two the growths have been held in check, while one was only temporarily benefited. In the same paper he reports his observations upon four other very severe inoperable cases which had been referred by him to other experts in radiotherapy. One has been apparently cured; one is still under treatment, greatly improved, and one (osteosarcoma) has been much benefited, the tumor being reduced in size, the pain relieved, and the general health improved. In one case there was failure.

Coley thinks there is little evidence to prove that deeply-seated tumors in the abdomen and chest can be cured or benefited by radiotherapy, but hopes that with increasing knowledge and skill with the apparatus even these may come within the beneficial influence of the treatment.

He repeats that the employment of the treatment has been too recent to claim that the healed areas are permanently cured and that the disease will not return. He finds its greatest application in cases of lupus and superficial cancers in the region of the face and neck, where the usual surgical measures are always accompanied by marked scarring and destruction of the tissues.

The results of radiation in treating *acne* are favorably considered by R. R. Campbell,[1] and William A. Pusey.[2]

In Campbell's fifteen unselected cases the results were uniformly good, nearly all were markedly improved from almost the beginning, and the majority were cured. In one case the results of treatment were delayed. After thirty-three exposures during three months, there being no apparent benefit, treatment was given up, but a month later the acne almost entirely disappeared.

No medication was employed in any of the cases quoted. Campbell used a medium soft tube, with a weak light, varying the time and distance of the applications. He strongly urges the necessity for care and caution. No case of acne treated for a reasonable length of time by

[1] Journal of American Medical Association, August 9, 1902.
[2] Journal of Cutaneous and Genito-Urinary Diseases, May, 1902.

Pusey with the rays has failed to derive benefit. He also used a very weak light, with a current just strong enough to illuminate a fairly soft tube. He warns all who wish to use the treatment to employ none other than the weakest light and to suspend treatment upon the first appearance of erythema or pigmentation. Many writers incidentally mention the analgesic properties of the rays, but this subject is especially considered in a convincing publication by Seabury W. Allen,[1] who reports eight cases in which analgesic effects were pronounced.

The cases reported include one of chronic rheumatic arthritis, one of malignant growth, one of tubercular arthritis, one a fracture of the bones of the ankle, one a wound of the foot, one of varicose ulcer of the leg, one of ulcer of the foot, and one of tubercular sinus of the neck.

In several of these cases the X-rays had been used for diagnostic purposes, but were the means of very greatly alleviating the pain.

Serums. ANTIPLAGUE SERUM. We must consider antiplague serum still in the experimental stage, although it is highly praised by some who have employed it in a limited number of cases. During the recent epidemic of plague at the Ile de la Reunion, eighteen cases were treated with the serum, and the results reported by J. J. Vassal,[2] the chief of laboratory of bacteriology on the island. The death-rate in fifty-one patients not treated with the serum was 80.3 per cent.; while in the eighteen other patients who were treated it was only 38.8 per cent. An average of 169 c.c. of serum was used upon each patient. A child, aged ten years, who was seriously ill and recovered, received during the illness a total quantity of 440 c.c. of serum. In some cases as much as 40 c.c. was injected at a single dose into a vein. Vassal believes that the favorable results were secured by the use of large doses. Dr. Frederick G. Novy[3] reports the case of a young man, who, while working with a highly virulent culture of the plague bacillus, was accidentally inoculated, developed acute primary pulmonic plague, and recovered under treatment with the Yersin antipest serum. The patient became ill during the morning of April 4th. At 4 P.M. of the same day he was injected subcutaneously with 20 c.c.; at 11 P.M., intravenously with 20 c.c. The following day his temperature was still high, and 20 c.c. were administered intravenously, and 40 c.c. subcutaneously, making a total quantity of 120 c.c., of which 60 c.c. were given intravenously during twenty-four hours. Within a few hours after the last injection the temperature dropped to 100° F., and before the third day reached the normal. Cardiac weakness persisted for more than two months.

[1] American Medicine, March 22, 1902.
[2] Intercolonial Medical Journal of Australasia, April 20, 1902.
[3] American Journal of the Medical Sciences, October 5, 1901.

ANTIPNEUMOCOCCIC SERUM. The clinical value of antipneumococcic serum is still inconclusive. The claims of enthusiasts that acute croupous pneumonia could be aborted by the use of the serum have not been verified, and the most now claimed by those who favor a further trial of the alleged remedy is that by its use the symptoms are favorably modified and the death-rate slightly lowered. Even these modest assertions have not been accepted by some competent observers, who, with unbiased minds have employed the remedy upon series of cases. Several hours after subcutaneous injections of 20 c.c. (if the fever is high) there is usually a temporary fall of one or two degrees in the temperature, but it is denied that the fever can be kept down continuously by repeated doses. There is also some conflict of opinion as to whether pleural pains are lessened by the use of the serum. In order to subject it to a fair but rigid test, Dr. G. G. Sears[1] selected twelve cases in which it was thought the effect of the serum could be estimated. No hopeless cases, nor those in whom the prognosis was particularly favorable, were selected, but only severely ill patients were subjected to the treatment. In addition to the serum, cold sponging, oxygen, alcohol, and other stimulants were employed. He was unable, even by most vigorous treatment, to abort the disease in a patient who had been ill two days. The duration of the disease was not lessened, and no appreciable permanent reduction of temperature was noted. In three of his cases there was an extension of the pneumonic process during serum treatment. He did not find it a specific against pain, and yet patients were peculiarly comfortable. In one case pleural pain was a distressing symptom throughout the illness in spite of the fact that large quantities of serum were used. Four of the cases ended fatally, so there could be no claim of a reduced death-rate. Skin eruptions, together with painful and swollen joints, were occasionally produced. Considering the severity of his tests Sears thinks the remedy entitled to further trial. While the serum did not precipitate the crisis in any of the six cases subjected to the treatment by Joseph Eichberg,[2] the severity of the symptoms seemed to be modified by it. One patient died upon the sixth day of the disease, four days after the treatment was instituted. Dr. Brice W. Goldsborough[3] enthusiastically advocates the serum treatment, and states that he would feel culpable to a great degree if he should treat a case of pneumonia without it, especially as it is harmless, and does not interfere with the use of other remedies. He reports nine cases with two deaths where this treatment was employed. In all the cases reported there was marked improvement

[1] Boston Medical and Surgical Journal, December 12, 1901.
[2] American Medicine, April 26, 1902.
[3] Journal of American Medical Association, June 28, 1902.

within eight hours after the administration, and in some the crisis was successfully passed within forty-eight hours. He states that the usual death-rate from pneumonia in the hospitals of America is from 25 per cent. to 35 per cent., and that collected statistics of 386 reported cases treated with antipneumococcic serum gives the death-rate of 16.5 per cent.

ANTISTREPTOCOCCIC SERUM. The therapy of *puerperal fever* is still unsatisfactory, and, judging from clinical reports, antistreptococcic serum has not materially lessened the danger in these cases. The remedy is applicable to cases of pure streptococcic infection only, and it cannot be expected to prove of value in severe cases of mixed infection or when infected clots fill the uterine veins. The serum appears to have been used with more success in the treatment of other cases of streptococcic infections. R. I. Chipman[1] employed the remedy with marked success in a case of *acute articular rheumatism* with pyæmic temperature. Before serum treatment was instituted the patient was greatly prostrated, both physically and mentally, and seemed to be rapidly progressing toward a lethal ending. After the first injection there was marked improvement in the general and local symptoms, and after seven days of treatment, during which time seven injections of serum in doses of 10 c.c. (f℥ijss) each were administered, the patient was entirely out of danger, and convalescence was uninterrupted except for a rather severe attack of urticaria.

Cooper and Ogle[2] report a case of *infectious endocarditis* with a rheumatic history, in which rapid, marked improvements in temperature followed the use of the serum. For a time the patient seemed to be convalescent, but on about the eighth day became prostrated, and died suddenly three days later. Lambinon,[3] in reviewing the subject of serum treatment of *puerperal sepsis*, states that the serum should be given in daily doses of 10 c.c., and continued so long as the temperature and the pulse range remain high. He also states that the bacteriological examination should be made in every case, but that the serum may be used, even when no such examination has been made, provided that antiseptic and surgical treatment are instituted at the same time. The value of the serum in the treatment of *erysipelas* is favorably commented on by A. Joss,[4] Hobart,[5] and Robert Leudeking.[6] Hobart and Leudeking also experienced good results from the use of

[1] Philadelph Medical Journal, June 28, 1902.
[2] British Medical Journal, May 10, 1902.
[3] Semaine Gynécologique, January, 1902.
[4] Corresp. Blatt. f. Schweizer Aerzte, October 1, 1901.
[5] Boston Medical Journal, December 12, 1901.
St. Louis Courier of Medicine, April, 1902.

the serum in cases of streptococcic infection in *suppurations of the middle ear.* Collins states that his experience with the serum in the treatment of erysipelas is equally efficacious when given by the rectum. The serum has been employed by Hunter[1] with benefit in treating three cases of *pernicious anæmia.* It is his belief that streptococci are the most virulent micro-organisms that occur in the mouth, and consequently the most important in the production of the gastric septic conditions. In the three cases treated by him there was a remission of the symptoms of pernicious anæmia, while the patients were under observation.

ANTITYPHOID SERUM. The results secured from the use of diphtheria antitoxin have been so remarkable as to stimulate numerous investigators to produce sera which would be preventive and curative in various other infectious diseases. Much patient work has been done in attempts to find a serum that would be of value in typhoid fever, but as yet these efforts have been unsuccessful. Ehrlich believes that the failure to produce a typhoid antitoxin is due to the fact that the sera experimented with have been derived from species of animals so distinctly removed from man that the amboceptors of the animal sera cannot find their special complement in human serum. Others are inclined to attribute the failure to the fact that typhoid fever is not a toxæmic disease, but a septicæmia or bacteriæmia, and that a serum to be of value is not necessarily antitoxic, but must be bactericidal. As if to further complicate the problem, it appears that the bacillus typhosus is so altered in its character by the colon bacillus and other species intermediate in their characters between typhosus and coli (which it meets in the intestinal canal), that a serum which is bactericidal against a pure culture of typhosus only will not favorably affect the course of typhoid fever. Thus, a serum to be of value in preventing and curing typhoid should be bactericidal in the blood to bacillus typhosus, bacillus coli, and the intermediate groups. Considerable work in the production of such sera has been carried on by Bokenham, Walker, Savel, and others. E. Chantemesse, by cultivating typhoid bacilli upon the filtrate of splenic extract emulsion in the presence of pepsin, and excluded from air, claims to have developed an extremely active and specific typhotoxin with which horses may be so immunized that their serum becomes strongly bactericidal and both preventive and curative for animals. The serum prepared by him has been employed in the treatment of one hundred cases of severe typhoid fever, and the reports[2] are most favorable. It is claimed that as a general rule within

[1] Proceedings of New York Academy of Medicine; Medical News, January 11, 1902.
[2] Bulletin de la Soc. des Hôp. de Paris, November 21, 1901.

thirty-six to forty-eight hours after the injection there is a fall in the temperature, accompanied by an improvement in the general condition of the patient. The doses of serum injected range from 4 to 12 c.c. (f℥j to f℥iij), usually only one injection is required, but if necessary may be repeated after several days. The cold-bath treatment is directed to be employed in conjunction with the serum.

ANTIVENOMOUS SERUM. As is well known, the venom of poisonous serpents contains two severely toxic principles. One, a peptone, which gives rise to systemic symptoms through its action upon the central nervous system, principally the centre of respiration. The other toxic substance is said to be a globulin. Its action is almost if not entirely local; and when injected into the subcutaneous tissues it is severely irritating and devitalizing, causing extravasation of blood with necrotic and gangrenous changes. The relative quantities of these poisons differ greatly in the various species of serpents. For instance, that of the cobra contains large quantities of the peptone or nervous poison and small quantities of the globulin or local irritant and disorganizer; while the venom of the rattlesnake is rich in the globulin. In attempting to immunize horses against rattlesnake venom, McFarland[1] found that while the animals could be immunized with comparative ease to the peptone poison they could not be against the globulin, even after long-continued injections. The tissues of the animals did not become less susceptible to the destructive action of the poison, nor was the serum of the animals treated protective when administered to other animals. As the antivenene of Calmette protects powerfully against the nerve poison of venoms, but not against the irritating poison, he considers it more useful for the bites of cobras and columbine serpents than vipers. In the past considerable difference of opinion has existed as to the action of snake venom upon the coagulability of the blood; some authorities contending that it rendered the blood incoagulable, while others held that the coagulability was markedly increased. The experiments of Lamb[2] have done much to harmonize these conflicting opinions, and have shown that non-lethal quantities of venom lessen the coagulability of the blood, while lethal quantities markedly increase it; and he believes that death, in rapidly fatal cases, is due to thrombosis of the pulmonary arteries. In an exhaustive research which distinctly proved that snake venom possessed agglutinating, hæmolytic, and antibactericidal power, Flexner and Noguchi[3] also tested the effect of antivenene upon venom and venomized blood, and found that

[1] Journal of American Medical Association, December 14, 1901.
[2] Indian Medical Gazette, December, 1901.
[3] University of Pennsylvania Medical Bulletin, February, 1902.

it neutralized venom and removed both its hæmolytic and antibactericidal action.

SERUM THERAPY IN EPILEPSY. An entertaining essay upon this subject, by Dr. Carlo Ceni,[1] of Reggio-Emilo, Italy, was awarded the Craig Colony Prize in 1901. In this paper the full clinical histories of ten cases of severe idiopathic epilepsy treated by the injection of serum obtained from the venous blood of epileptics are given. None but severe cases were selected for experimentation; and of these, two were cured, six decidedly improved for a time, and more or less permanently benefited, and two were temporarily made worse and not ultimately benefited. The effect of the treatment appeared to be influenced by the hereditary nature of the disease, the age of the patient at the time of its development, and its duration at the time serum therapy was begun.

The two patients who were cured had been afflicted only three years when the serum treatment was instituted, and were without hereditary taint. The two cases in which the treatment was negative were hereditary. The mother of one was an epileptic, and the patient, aged nine years, had been afflicted since three months of age. In the other case both parents were epileptics, and the patient had been similarly affected since early childhood. In the six cases which were benefited but not cured, hereditary stigma was either absent, or, if present, the epilepsy had not developed until the patient had reached puberty. All of the six, however, had been subject to epileptic manifestations for from ten to twenty years. In the improved but not cured cases the beneficial effects of the serum were more lasting in the young than in the old patients. Those who were cured gained rapidly in weight, patients who only improved gained in weight more slowly, while those not benefited progressively lost weight coincident with exaggeration of the epileptic phenomena. The method of obtaining and applying the serum was as follows: Under strict antiseptic and aseptic precautions venous blood was withdrawn from carefully selected cases of severe epilepsy, and after separating the serum it was preserved by prolonged factional sterilization and the addition of camphor. In most instances the serum was obtained from the blood of epileptics more severely afflicted than those to be treated, but some of the patients were treated with serum taken from their own blood. The serum of non-epileptics was tried upon other patients, but was found not to be therapeutically active. At the beginning of treatment injections into the glutei of from 3 to 5 c.c. of serum, at intervals of several days, was usually followed by an "accommodation reaction," during which time the patient

[1] Medical News, March 8 and 15, 1902.

often became temporarily worse. After about four weeks of such treatment the "accommodation reactions" ceased, and larger quantities of serum could be employed without giving rise to disagreeable symptoms. After toleration was established as much as a total quantity of 50 to 100 c.c. of serum could be given during each month. In all cases benefited there was improvement in the weight, color, digestive functions, mental and moral condition, as well as a lessening of epileptic manifestations. In the cured cases the improvement was progressive, rapid, marked, and uninterrupted; in those only benefited it was intermittent, slower, interrupted, and, after a time, ceased; while in those not benefited by the treatment there was loss of weight and an exaggeration of all the epileptic phenomena, from the very beginning until it was discontinued. All the patients did not experience disagreeable effects at the beginning of treatment, and none subjected to autotherapy manifested symptoms of "accommodation reaction." From previous study and experimentation of the pathogenesis of epilepsy, Ceni believes that the epileptic phenomena are the consequence, at least for the greater part, of toxic products circulating in the organism. He is not in accord, however, with the theory that the periodic epileptic crises result from a periodic increased production or accumulation of these poisons. He states that by experimentation he has proven that the quantity of the epileptogenic substance circulating in the blood does not change at different stages of the disease, and he advances the thought that "the epileptic phenomena are brought about by a discharge of dynamic energy, gathered in epileptogenic centres, in consequence of an irritation, lasting, constant, and uniform for an indeterminate time." The serum of epileptics is said to contain two active principles which are capable of deeply modifying nutrition and epileptic manifestations, one of which is said to circulate in a free or uncombined state, and is endowed with toxic properties only when injected into other epileptics, and which gives rise to the reaction of accommodation. The other active principle circulates in the blood of epileptics only in a latent state, and when injected stimulates the metabolic cells concerned in the elaboration of the epileptogenous poison. The beneficial effect of the serum he believes is probably brought about by its power to favorably modify the metabolic changes in the cellular elements which elaborate the epileptogenous toxin, lessening the quantity in some cases and causing its disappearance in others. The failure of the serum in some cases he thinks may be attributed to the fact that in these subjects the cellular elements of the body concerned in the elaboration of the toxin are in a condition to deprive them of the power to react physiologically with the serum. Under the stimulating influence of the principles contained in the serum they become pathologically hypersecretive,

resulting in an increase of the epileptogenous toxin, and a consequent deterioration of the patient.

SERUM THERAPY IN SCARLET FEVER. The proof that Marmorek's antistreptococcic serum, serum taken from patients convalescent from scarlet fever, or diphtheria antitoxin, are valuable in treating patients ill with scarlet fever, is far from convincing. All have been, to some extent, favorably reported upon, but none has been generally accepted or extensively employed. It is confidently hoped, and there is good reason to believe, that for a disease like scarlet fever, in which one attack usually renders the subject immune to others, a reliable antitoxin or serum which will favorably modify the symptoms and may also be employed as a prophylactic against the disease will sooner or later be discovered. Very recently, Moser[1] published the results of his experience with serum taken from the blood of horses injected with progressively increasing doses of living culture (grown on bouillon) of streptococci taken from the blood found in the hearts of patients dying of scarlet fever. His experience with other antistreptococcic serums has not been satisfactory, and he believes that streptococci found in the heart cavity of children dying from scarlet fever differ from those found in erysipelas and other streptococcic infections. The serum upon which Moser reports was made at the official Institute for Serum Therapy in Vienna, and was used in treating only the severest cases of scarlet fever at the St. Anna Hospital.

By injecting subcutaneously large quantities of this serum, it is claimed that the course of the disease was shortened, the symptoms controlled, and the death-rate lowered. I say in large quantities, for doses of 10, 20, or 30 c.c. were found to be insufficient, and injections of 180 c.c. were usually required and came to be employed as the current dose. It is stated that after full doses, patients extremely ill quickly and decidedly changed for the better. The eruption either did not come to full development or disappeared rapidly. The nervous symptoms were controlled; the temperature declined more quickly than is usual in such cases; respiratory and pulse-rates were lowered, and the tendency to cardiac weakness was counteracted. Gastro-intestinal symptoms were controlled within twenty-four hours, and swellings in the nasopharynx were relieved. It is not claimed that superficial necroses were prevented, but it is stated that extensive destructive processes in the throat no longer occurred. None of the cases treated developed chronic septic intoxication, but pyæmic conditions were occasionally noted. Although no very definite conclusions could be reached, it was thought that nephritis was less common than usual. With the

[1] Wiener klin. Wochenschrift, October 9, 1902.

exception of the development of eruptions and joint pains (as from the use of full quantities of all serums taken from the blood of horses) in some cases, and of abscesses at the seat of injection in a small percentage, there were no harmful effects observed from use of serum in any of the eighty-one cases treated with it. The report of Moser is encouraging, but members of the medical profession have become somewhat skeptical concerning the value of the newer serums which are being constantly brought to their notice. More extensive trials and further reports will be patiently awaited.

Soluble Silver (Collargol). The reputation of soluble silver (collargol) in the treatment of septic processes rests entirely upon clinical evidences, for although Schlossmann claimed that it was an active bactericide, Gindes and Balerdzsheff found it to be a very feeble one. The remedy needs further scientific study, but clinical reports attesting to its value as an internal antiseptic continue to multiply. The remedy is usually applied locally in the form of an ointment, but it is claimed to be equally effective in many cases when given by the mouth in pill form, and in urgent cases hypodermically or intravenously. Intravenous injections are usually followed by rather marked reactions in which there is a rise of temperature or chills. If administered by the mouth it sometimes gives rise to gastric disorder, so that, as a rule, inunctions are preferable to other methods of administration. Inunctions are best made by first washing the skin with warm water and soap and disinfecting with alcohol; then rubbing the ointment in for twenty to thirty minutes. The experience of G. Woyer[1] leads him to believe that soluble silver is a remedy of considerable value in gynecological practice. Three cases of *puerperal septicæmia* are reported by him, in which, after inunctions with Credé's ointment, improvement was so marked that, while fully recognizing the irregular course of such cases, which often improve without treatment, he thought the results should be ascribed to the remedy. D. Fisher[2] states that during the past two years in treating septic infections when not practical to apply the ointment, he has used intravenous injections of soluble silver with good effects. He reports a severe case of *anthrax of the face*, in which the diagnosis was confirmed by microscopic and bacteriologic study, that was cured by three injections into the cephalic vein of 5 c.c. doses of a 1 per cent. collargol solution. The intravenous injection of soluble silver, of which he uses 1 to 5 c.c. of a 1 per cent. solution at a dose, is regarded by J. Müller[3] as a specific in septic affections. He has employed the treatment in thirty cases, including cases of

[1] Münchener med. Wochenschrift, October 15, 1901.
[2] Ibid., November 19, 1901. [3] Deutsche med. Wochenschrift, March 13, 1902.

threatened erysipelas, extensive cellulitis, mastitis, pelvic exudates, lymphangitis, and tuberculous arthritis. Improvement followed in all his cases after a single injection, but in seven cases several were given. No after-effects were noticed, excepting the chill, which usually came on in from one to four hours after each operation.

SILVER VITELLIN. Dr. L. D. Lederman[1] has, for the last five months, made use of this substitute for silver nitrate in the strength of from 5 per cent. to a saturated solution in treating acute and chronic disturbances of the nose, pharynx, and larynx, and *chronic purulent otitis media.*

He found it to possess all the good qualities of silver nitrate without any of its unpleasant, irritating features. Its superior therapeutic effects, he thought, should be attributed largely to its solubility and its increased power of penetration of the tissues.

Strychnine. There can be no doubt as to the great value of full doses of strychnine used to overcome sudden and profound cardiac depression, with vasomotor relaxation but its routine use in large doses; as a circulatory stimulant throughout the course of exhausting diseases is to be condemned. The wonderful effects noted as following the use of a few full doses of strychnine in surgical shock and collapse during acute illness seem to have been misinterpreted by many physicians. It became popular, a few years ago, to use full doses of the drug throughout the whole course of acute exhausting diseases, such as pneumonia, typhoid fever, and as a routine treatment for myocardial weakness. At the very height of what might be termed the "strychnine craze," Dr. H. A. Hare called attention to the abuse of the drug and of harmful effects likely to follow the continuous or routine use of full doses. He impressed upon his classes and members of the medical profession that strychnine is an irritant stimulant, which should be applied in a crisis only, a few doses at the most being given; and its continuous employment is like applying the whip to a tired horse, with the result that in the end less energy is developed. He also pointed out at that time, and again more recently,[2] that the continuous use of strychnine in typhoid fever, pneumonia, influenza, and similar exhausting diseases frequently produced not only an excess of nervous irritation (as irregular temperature and a rapid pulse), but also rendered patients unduly irritable, and, where exhaustion was extreme, may cause a certain amount of delirium. He does not condemn the use of the remedy in small doses as a bitter tonic and slight nervous stimulant during convalescence.

[1] Medical Record, November 29, 1902.
[2] Editorial, Therapeutic Gazette, January 15, 1902, p. 35.

The use and abuse of the remedy in treating *heart diseases* has recently been discussed by Dr. A. Jacobi and Dr. Roland G. Curtin. The routine application in heart disease is condemned by both of these gentlemen. Jacobi holds that owing to the pronounced effect of the drug upon the vasomotor system it is especially indicated in those cases in which the heart muscle is feeble and the blood pressure low. He emphasizes the fact that the vasomotor centre, like others of the medulla, is soon fatigued by over-stimulation, and if strychnine in full doses is continued too long the blood pressure will fall below the normal. He thinks it should be regarded as a temporary remedy, and while we may, in many cases of cardiac disease, rely upon it as a valuable stimulant to aid the reparative processes, it should not be looked upon as a specific, nor continued over long periods of time. Dr. Curtin[1] strongly opposes the use of large doses of strychnine in treating a heart "already crippled by diseases." The stimulating action of the drug upon the heart muscle is slight, as compared with its effect in raising arterial tension through its action upon the vasomotor system. He holds, therefore, that the work of an already weakened heart is increased by causing it to pump blood at a greater resistance into contracted bloodvessels. His opposition is based, however, more largely upon his clinical experience. He has never seen a "case of marked depression of the heart from chronic disease in an elderly person in which large doses of strychnine were given, and the patient survived," although he has often observed good effects in similar cases from the proper administration of alcohol, digitalis and other heart tonics. The views expressed by these well-known medical men will probably meet with opposition from many who use full doses of strychnine in treating circulatory depression under all conditions, and from whatever cause; but I am confident that a review of past clinical experiences and careful observations in the future will convince many that the alkaloid has been and is still very often used in excessive doses and for too long a period of time.

An interesting observation on the influence of the contents of the large intestine upon strychnine which may have some bearing in medico-legal cases has been made by Dr. William Salant.[2] He discovered that when 1 milligramme ($\frac{1}{60}$ grain) of strychnine was mixed with the contents of the cæcum and colon of rabbits no chemical reaction from it could be obtained, but when mixed with the contents of any other part of the intestinal canal or stomach there was no difficulty in detecting it by chemical tests.

Stypticin. Cotarnin Hydrochloride. This substance, which was originally introduced into medicine as a remedy for internal use in the

[1] Therapeutic Gazette, November 15, 1902.
[2] American Medicine, August 22, 1902.

treatment of oozing hemorrhages, and found particularly valuable in certain cases of *menorrhagia*, is said by R. Kaufman[1] to be equally valuable when used locally in oozing hemorrhages from mucous membranes.

In *urethral hemorrhages*, after passing bougies or the using of the endoscope, he found it very satisfactory and much cheaper than hydrastinine, for which it could be substituted. For use in urethral hemorrhage he recommends its application in the form of pencils, as follows:

℞.—Stypticini . . . . . gr. iij.
Olei theobromæ . . . . . ʒij.
Misce et ft. bacilli No. vi.
Sig.—Use one in urethra.

The suppositories are retained in the urethra by placing cotton over the meatus and holding it in position by drawing forward the prepuce or by means of a rubber band or condom.

The substance is said to act very satisfactorily in controlling hemorrhage following tooth extraction.

Stypticin is a yellowish powder, soluble in water and alcohol. Its dose by the mouth is from 2 to 4 grains; for hypodermic use about half that quantity. For controlling bleeding after extraction of teeth it should be applied pure or in 50 per cent. solution. The drug costs less than two cents a grain.

Suprarenal Gland and Its Active Principles. Investigation of these extremely interesting substances has given us a fair knowledge of their physiological actions. Although there are some chemical differences between *suprarenin* of Futh, *epinephrin* of Abel, and *adrenalin* of Takamine, there are no practical differences in their physiological actions. When suprarenal gland or its active principles are administered intravenously, intraperitoneally, or subcutaneously, their action is more prompt and powerful than when given by the mouth or rectum. The first two methods of administration should never be practised except under the most extraordinary circumstances, and, as when given subcutaneously, abscesses or sloughing frequently occur, the oral method is preferable. Locally applied to the skin, no noticeable effect is produced, but on mucous membranes or denuded surfaces there is a marked contraction of the capillaries, accompanied by blanching of the parts. This effect is more pronounced than with cocaine, but, not unlike that substance, the contraction is said to be followed, in some instances, by paralytic distention. The action of the drug upon the cerebrum is probably very slight, but in large overdoses restlessness is a marked symptom. In toxic doses there is a general loss of power,

[1] Monatshefte f. Praktische Dermatologie, February 15, 1902.

which is thought by Gourfein, Oliver, and Schäffer to be due to its effect upon the cord, but by Vincent to the action upon the muscles. Non-toxic doses exert no perceptible influence upon respiration, but in toxic doses death takes place by respiratory failure. It is stated by Gourfein that if respiration is artificially maintained there is a final loss of heart power, with paralysis of the vagi. The dominant influence of the drug is upon the circulation, which is decided when given intravenously, and somewhat less when administered subcutaneously. It is still less pronounced when given by the mouth or rectum. After intravenous injection there is a sharp rise in arterial pressure and an increase in the force of the heart, and slowing of its rate. These effects are very fleeting, and do not last over ten minutes. The rise in pressure is due to stimulation of the vasomotor centre, stimulation of the coats of the bloodvessels, and to increase in the force of the heart-beats; while the slowing is caused by stimulation of the vagi. The effect upon circulation is similar in kind to that of digitalis, but unlike this latter drug it comes on promptly and passes away quickly. Both voluntary and involuntary muscles are stimulated by moderate doses and paralyzed by toxic quantities. The active principle is said by Cybulski to be eliminated by the kidneys, but Langlois believes it is largely oxidized in the liver. That *glycosuria* could be developed in animals by subcutaneous injection of suprarenal substance was first announced by Blum,[1] and was soon thereafter confirmed by A. C. Croftan,[2] and C. A. Herter and A. N. Richards.[3] Both Blum and Croftan believe that the suprarenal gland contains a diastatic ferment which converts the glycogen of the liver into sugar. Herter and Richards strongly oppose this veiw, theirs being that glycosuria is caused by the reducing action of the active principle of the gland upon the cells of the pancreas. Herter and Richards showed by elaborate experiments that a more pronounced glycosuria could be instituted by intraperitoneal injection and local application to the pancreas than by any other method of administration. Subcutaneous injections, according to I. N. Langley,[4] increase the secretion of the salivary glands, as well as those from the buccal œsophageal and tracheal mucous membranes.

Adrenalin possesses many advantages as a therapeutic agent over the crude gland or the extracts. It is said to be six hundred and twenty-five times as powerful as the gland, may be used in small and exact doses, and is easily sterilized by heat. This principle has almost entirely replaced all other products and preparations made from the

[1] Berliner klin. Wochenschrift, 1901, No. 48, p. 1209.
[2] American Medicine, January 18, 1902. [3] Medical News, February 1, 1902.
[4] Journal of Physiology, October 16, 1901.

gland. The therapy of the gland and its active principle were rather freely discussed in these pages a year ago, but we do not feel that the subject should be dismissed without calling attention to some of the diseased conditions in which it has been most recently used. No other remedy appears to have met with such uniform success in preventing and controlling *hemorrhage*. By spraying the cavities with a 1 : 1000 or 1 : 10,000 solution of adrenalin chloride, bloodless operations may be performed upon the nose (John P. Kyle, Flemming Carrow,[1] A. Stanley Green,[2] and G. Ferdinando[3]). It is true that after the effects of the drug wear off there may be some bleeding, but this is said not to be greater than in operations performed without it. Moreover, if it is desired to entirely prevent bleeding, the nasal chambers may be plugged after the operation has been completed. According to Grünbaum, *hæmophilia* is due to congenital hyperplasia of the muscular coats of the arteries, and, this being true, it is difficult to understand how suprarenal substances or its active principle could be of value in the treatment of the condition. The drug, however, is reputed to be of decided worth in controlling the bleeding in hæmophilics, and Thomas[4] has used it both locally and internally with such apparent success that he advises that "bleeders" should be provided with it, to apply, if occasion arises.

If a single drop of adrenalin chloride (1 : 1000) is injected under the skin there is a slight burning sensation, and immediately the skin within an area of one inch around the seat of the injection becomes blanched and bloodless, and remains in this condition about two hours. With weaker solutions the blanching almost entirely disappears in a much shorter time. Realizing that by adding adrenalin chloride to solution of cocaine or eucaine, local anæsthesia with these substances might be prolonged, and an operation rendered bloodless, Elsberg[5] has recently made use of the method in a number of minor operations, and states that he is well pleased with the result. To the cocaine solution he adds adrenalin chloride in the proportion of 1 : 5000 to 1 : 20,000. The amount of bleeding was remarkably slight, so that sponging was unnecessary and no sloughing was observed. In more than thirty clean operations, primary union was not interfered with nor delayed; and in only one case, the removal of a small sebaceous cyst from the scalp, was there any sloughing, and in this instance it was not thought that the adrenalin contributed to or caused the accident. It has been shown that if the absorption of cocaine is delayed after its injection into the

[1] Therapeutic Gazette, January 15, 1902.
[2] British Medical Journal, May 10, 1902.
[3] Ibid., March 22, 1902.
[4] Ibid., November 23, 1901.
[5] American Medicine, March 1, 1902.

tissues it almost entirely loses its toxic effect, and we can readily conceive how the addition of adrenalin could be of value in this respect also.

Solutions of adrenalin chloride have been used by Chassaignac[1] in the management of certain genito-urinary diseases. In *hæmaturia* a weak solution, 1 : 20,000 or 1 : 30,000, injected into the bladder, and permitted to remain five minutes, not only controls the bleeding, if its source is within this viscus, but also assists in determining whether the bleeding originated within the bladder or from the kidneys. He also uses the remedy locally, in some cases, to reduce engorgement within the urethra, thereby facilitating endoscopic examinations or permitting the passage of sounds. In cases of specific urethritis, after all infecting micro-organisms have disappeared, but in which, owing to congestion, there is a persistent mucous discharge, local applications have proved of value. Howard[2] states that in *acute specific urethritis* very satisfactory results have been secured by irrigation with 1 : 4000 solution of adrenalin chloride, followed by 1 per cent. protargol solution.

In the *Medical News*, January 4, 1902, Floersheim publishes twenty-one cases of *hæmoptysis*, twenty-three of *uterine hemorrhage*, and one case of *hæmatemesis*, in which he employed 15 grains of suprarenal gland every two hours. He states that he knows of no other remedy whose internal administration has given such prompt results, and that in his hands it has proven a safe remedy, even when the hemorrhage was complicated by diseases of the heart, lungs, and kidneys. He advises that the powder should be taken upon the tongue, moistened with the saliva, and swallowed without water. It occasionally causes nausea and vomiting.

The use of adrenal substances in the treatment of *intestinal hemorrhage of typhoid fever* has been strongly advocated by Warren Coleman.[3] He publishes five cases in which the remedy was successfully employed. Doses of 15 grains of adrenal gland three to six times a day are suggested. It is observed that the ice coil was also used. In the treatment of intestinal hemorrhage, Douglass MacDonagh[4] successfully employed enemata containing adrenalin chloride (1 : 1000). In view of the fact that nausea and vomiting sometimes follow the administration of suprarenal extract by the mouth, Adams[5] suggests that it may be given with equal advantage by the rectum. He cites a case of hæmatemesis in which 10-grain doses of the extract suspended in water, given by the rectum every two hours at first, and then every four hours, were successfully employed.

[1] New York Medical Journal, February 15, 1902.
[2] Mississippi Medical Record, April, 1902.
[3] Medical News, March 29, 1902.
[4] British Medical Journal, March 5, 1902.
[5] La Semaine Médicale, 1902, No. 4.

We can hardly conceive that adrenal extract when given by the mouth is sufficiently powerful in its action upon the heart to make it a valuable *cardiac stimulant*. It has been used, however, with asserted success by A. L. Benedict[1] in cardiac depression with vasomotor relaxation, and by Gray[2] in impending heart failure during pneumonia. It is stated that in some of the cases of pneumonia treated by Gray the beneficial effect was rapid and marked.

Tetanus Antitoxin. The early experiments with tetanus antitoxin on animals seemed to indicate that the agent would be of great value in treating tetanus in man, but these hopes have not yet been realized. Many recoveries from chronic tetanus under antitoxic treatment have been reported, but the value of the remedy must be based upon its power in acute cases. It is rather definitely settled that subcutaneous injections of the antitoxin in these latter classes of cases are extremely feeble or probably inert. We have previously called attention in these pages to the use of the serum by intracerebral and spinal subarachnoid injections, and it is interesting to note that these methods are still being tried. The reports concerning the results secured are conflicting. Letoux[3] considers subcutaneous injections valuable only as a preventive, but intracerebral injections curative in many cases. The early use of full doses (20 c.c.) he regards as imperative. Not less than twenty minutes should be consumed in making an injection into the motor area of each hemisphere. E. v. Leyden[4] collected from the literature twenty-four cases, with six recoveries after treatment by intracerebral injections; and eleven cases, with five recoveries after spinal subarachnoid (dural infusions) injections. The technique of dural infusion is the same as for lumbar puncture, but Leyden states that the treatment to be successful must be accompanied by the use of narcotics. The intraspinal injection of 10 c.c. of serum under chloroform anæsthesia is considered by N. D'Ancona[5] the best method of administration. Two cases thus successfully treated are described. The spasms increased in frequency and severity immediately after the first injection, but in a few hours there was noticeable improvement. The injections were repeated at intervals of three or four days, and in each case a total of four injections were given. After the second injection fever subsided, convulsions were less frequent, and only slight muscular rigidity remained. Improvement was still more marked after the third and fourth injections, and the ninth-day convalescence was established. The seat of infection was excised in both cases.

[1] Therapeutic Gazette, October 15, 1901.
[2] Medical Record, April 5, 1902.
[3] Presse Médicale, October 30, 1901.
[4] Therapie der Legenwart, August, 1901.
[5] Gaz. degli ospedali e clin., November 24, 1901.

T. Pfeiffer[1] believes the best results are to be obtained by spinal subarachnoid methods, and reports fourteen cases treated by himself with a mortality rate of 50 per cent.

Theobromine, like caffeine, stimulates the secreting epithelium of the kidney, and is a diuretic of considerable power.

This alkaloid and its preparations are much more expensive than caffeine, and it is extremely doubtful whether, except under special circumstances, as, for instance, when there is gastric irritability, it is of equal value or possesses any advantage over that substance.

In addition to the sodio-salicylate of theobromine, which has been in use for several years, the newer compounds uropherin B., uropherin S., and agurin seem to act well in certain cases.

UROPHERIN B. is theobromine-lithium and lithium-benzoate. It appears as a white powder, soluble in water, but readily decomposed by it, and should, therefore, be prescribed in capsules. As may be judged by its composition, this compound of theobromine is indicated in *phosphaturia* as a diuretic and as a uric acid solvent. Its dose is about 15 grains.

℞.—Uropherin B. . . . . ʒij.
Pone in capsulas No. xxiv.
Sig.—Two to three capsules three times a day.

Thiosinamine. Thiosinamine appears as colorless crystals having a faint, garlicky odor and a bitter taste. It is soluble in water, ether, alcohol, and glycerin. When dissolved in water alone it quickly decomposes; but in a mixture of water and glycerin, remains unchanged sufficiently long to render it a good solvent for all practical purposes. The crystals are obtained by the addition of alcohol and ammonia to the volatile oil of mustard or horseradish, and the application of heat.

When administered by the mouth or hypodermically there is for a few hours a great reduction in the number of leucocytes, followed later by a very remarkable increase in number over the normal of these corpuscles. Considerable smarting or irritation, with swelling and hyperæmia at the seat of the puncture, immediately follows the hypodermic injection of thiosinamine dissolved in alcohol, or solutions of it in a mixture of glycerin and water give rise to little pain; the development of abscesses, however, at the seat of injections are of frequent occurrence, regardless of what solvent is employed.

The most remarkable action of this drug, and the one to which it owes its therapeutic value, is its power to produce swelling, softening, relaxation, and, in many instances, subsequent absorption of feebly-

[1] Zeitschrift f. Heilkunde, February, 1902, xxiii.

nourished pathological tissue, such as gives rise to cicatrices, overgrowth of fibrous tissue, or old inflammatory structures.

This property of the drug has led to its use for removing keloids or bring about a diminution in their size, for rendering unsightly scars less prominent, for relaxing œsophageal and urethral strictures, for removing corneal opacities, and for improving the hearing and relieving tinnitus when due to fibrous thickening within the middle ear or Eustachian tube.

The drug is said to be contraindicated in persons having a latent focus of tuberculosis and in those convalescing from articular rheumatism. In treating *keloids*, the best results seem to have been obtained by injecting the remedy into or about the dense tissue; but in all other conditions for which it is used it appears to act equally well, whether given hypodermically or by the mouth. For hypodermic use a 10 per cent. solution in water and glycerin, in doses of from about 10 to 20 minims every third or fourth day, is employed.

For administration by the mouth, from 3 to 4 grains a day is the usual dose.

F. Juliusberg[1] employed thiosinamine in a number of cases in which there had been marked scarring from *lupus*, keloids, and similar conditions, with most satisfactory results. He states that in some instances keloid and lupus scars have been practically entirely absorbed, and in *scleroderma* the board-like regions of skin have rapidly become soft and flexible. He made use of a 10 per cent. solution of the drug in water and glycerin, of which from 3 to 10 minims were injected in the scapular region every day. While the injections were usually painless, some patients occasionally developed urticaria or xanthema after its use.

Being impressed by the action of thiosinamine to produce softening and relaxation of cicatricial tissue, Henry S. Upson[2] conceived the idea of using it for relaxing stiffened joints in chronic rheumatic subjects, and for relieving painful conditions due to cicatrices about nerve trunks. The beneficial effects of the drug seemed to be marked in a patient with a stiffened wrist and atrophy of the muscles of the forearm following rheumatism, but in the other five cases reported there appears to have been but slight effect.

L. Teleky[3] states that the treatment of *œsophageal stricture* by dilatation alone is accompanied by a mortality-rate of about 55 per cent., and those treated surgically about 40 per cent. The most unsatisfactory cases of œsophageal stricture are those which improve by gradual dilatation only up to a certain point. The value of thiosinamine in treating urethral stricture suggested to him its use in this class of cases.

[1] Deutsche med. Wochenschrift, August 29, 1901.
[2] American Medicine, January 25, 1902.
[3] Wiener klin. Wochenschrift, February 20, 1902.

The first case treated was that of a woman with a fibrous œsophageal stricture, in whom at the beginning of treatment by dilatation it was only possible to pass a fine catgut sound, but after six months' treatment had been benefited so that a No. 16 bougie of 9½ millimetres diameter could be passed. As no further dilatation could be secured after another six months' treatment, it was decided to use hypodermic injections of thiosinamine. After ten treatments there was but little difficulty experienced in passing a No. 22 bougie of 12⅔ millimetres diameter. The woman could swallow well, and after a year's time there has been no relapse. Equally good results were obtained in another case in which the stricture had existed since childhood. In the case of a boy, aged twenty-eight months, who had drunk caustic potash six months before, after six injections a No. 21 bougie (12⅓ millimetres in diameter) could be passed, though previously none measuring over 9⅓ millimetres in diameter could be inserted. The improvement in swallowing, however, was less marked than in the other two reported cases. The treatment failed in a case of a boy, aged three and one-half years, who had drunk a solution of caustic potash only six months before. The fifth case was that of a man suffering with œsophageal stricture due to carcinoma, and upon whom it was necessary to perform gastrostomy. About the twelfth day after the operation a single dose of thiosinamine was administered hypodermically, with the hope of rendering the stricture permeable. A few hours later the healed gastric fistula became loosened, and the stomach wall separated from the abdomen under the influence of the drug, which was being administered to render the stenosis of the œsophagus permeable. The result was fatal to the patient.

A study of these cases show that the indications for thiosinamine injection in œsophageal strictures are strictly limited. Old cicatricial strictures were rendered soft and distensible, more recent cicatrices were first softened, but, if the treatment were continued, underwent inflammatory swelling, which rendered the strictures tighter than before. Quite recent cicatrices, as in the case of the gastrostomy wound, becomes so soft that they break down.

George F. Suker[1] used the remedy with very gratifying results in treating cases of *corneal opacities*, *ectropions*, and *choroidal exudations*. When the opacity was due to a true cicatrix thiosinamine was not capable of doing much good, but was of very great value, if due to an infiltrate or exudate pure and simple.

Taking into account the effect of thiosinamine upon feebly-nourished, pathological tissue, Dr. Joseph C. Beck,[2] and Dr. Lewis S. Somers[3]

[1] Journal of American Medical Association, August 9, 1902.
[2] Laryngoscope, June, 1902. [3] Merck's Archives, November, 1902.

were led to employ the drug in treating cases of *impairment of hearing* and *tinnitus*. The remedy seemed to be indicated in those aural affections in which there are sclerotic changes in the tympanic mucous membrane, with restriction of the movements of the membranæ tympani and ossicular chain, associated with more or less local thickening of the walls of the Eustachian tubes.

In the first five cases of chronic catarrhal *otitis media*, with impaired hearing and tinnitus, treated by Beck with thiosinamine, no other measures were employed, and, though continued for periods of time varying from three months to a year, the only good which seemed to result from its use was that the tinnitus became bearable and somewhat changed in character. In nine other cases treatment by thiosinamine was combined with electrolysis of the Eustachian tube, local treatment of the nose and throat, Politzerization, massage of the drum, and attention directed to improving the patient's general health.

It was necessary to continue the treatment from two to eight months, depending upon the rapidity of the improvement.

The conclusions of Beck based upon his observations of all the cases treated with thiosinamine were that without mechanical treatment the drug does not improve the condition except to produce some amelioration of tinnitus; with both thiosinamine and electrolysis, bougies could be passed with much greater ease and within a shorter time than without them; and, finally, that all cases treated with both of them improved in from two to eight months in all respects.

When thiosinamine treatment is instituted Somers thinks if there is no improvement after six weeks it is fairly probably that it will prove useless in that particular case. However, no hard-and-fast rules should be insisted on, for while some cases, especially of Eustachian stricture of two years' duration, react quite readily, other cases of longer duration present no apparent beneficial results for several months, then the catheter will demonstrate marked evidences of softening of the fibrous tissue. To be of maximum value, he holds that thiosinamine treatment should be accompanied by other measures directed to improve the patient's general health, removal of abnormalities of the upper respiratory tract, and to rendering the Eustachian tube patulous by Politzerization or by the passage of bougies.

In twelve cases of impairment of hearing, due to middle-ear sclerosis, associated with thickening of the walls of the Eustachian tube treated by Somers, the method of administering the drug was by the mouth, and in doses of from ½ to 1 grain, three times a day, in capsules or powders. Thus given it rarely produces untoward effects, and could be used for long periods of time, in most instances with the production, to a greater or lesser degree, of the therapeutic effect desired.

The hypodermic method seemed to possess no special advantages, while the oral method is much more convenient in this class of cases, which require long-continued treatment.

UROPHERIN S., or theobromine-lithium and lithium-salicylate, is a white powder soluble in but decomposed by water. It seems to have been used with a certain degree of success as a diuretic in *rheumatic* subjects. It should be prescribed in powder or capsules.

℞.—Uropherin S. . . . . ʒij.
Ft. chart. No. xxiv.
Sig.—Two to three powders three times a day; to be followed by a large draught of water.

AGURIN. This substance is a white, crystalline powder, soluble in aqueous liquids, and decomposed by acids. It is offered as a substitute for the diuretic theobroma salicylate, and on account of containing a larger percentage (60 per cent.) of the base is said to be active in smaller doses. It may be prescribed in doses of from 2 to 15 grains in aqueous liquids, in capsules, or cachets.

℞.—Agurin . . . . . ʒj.
Pone in capsulas No. xii.
Sig.—One capsule every three hours.

℞.—Agurin . . . . . ℈iv.
Syrupi . . . . . fʒj.
Aquæ cinnamomi . . . . . q. s. ad. fʒviij.
M. Sig.—Tablespoonful in water every three hours.

Thyroid Extract. Recent observations appear to confirm the belief that diseased conditions associated with athyroidea may develop not only from an absence of the gland or a pathological condition of its structure, but also from functional disturbances of its secretions. Dr. J. G. Perry[1] called attention to a combination of symptoms which he believes to be due to functional deficiency of thyroid secretion, and which may be benefited by the administration of thyroid gland. As the most prominent symptom of this disorder is pain in one or more joints, it is likely to be mistaken for rheumatism or suppressed gout. In fact, several cases coming under his care had been diagnosed as such, but had persistently grown worse until some preparation of thyroid gland was administered. The other symptoms usually present are generalized headache, rapid and enfeebled heart action, nervous irritability, and in women menorrhagia. The joints are not excessively tender, nor are they red or hot, but there is pallid swelling, with slight tenderness, resembling the so-called "neural arthropathy" described by Charcot.

[1] Medical News, November 16, 1901.

In his most typical case the urine was negative, although carefully examined to ascertain if there was an excess of uric acid or urates. The diagnosis is, to a certain extent, made by subjecting the patient to a therapeutic test with some preparation of thyroid gland. As he has demonstrated, they will bear large doses of this substance without showing symptoms of thyroidism. The etiology of the disease closely resembles a shock to the nervous system. One of his typical cases dated her illness from a time when she received a severe nervous shock. Some of the cases responded slowly at first to the thyroid treatment, but all were ultimately benefited in a marked degree. In fact, they were practically well as long as the thyroid gland continued to be administered.

After six years' experience, Georges Thomas Beatson[1] states that he has every reason to be well satisfied with the method originally suggested by himself, of treating cases of *inoperable cancer of the breast* occurring before the menopause, by performing oöphorectomy and administering full doses of thyroid extract In his recent paper he presents the results secured in his own practice, and quotes the opinions of a number of other surgeons who have successfully employed the method. He also raises the question as to whether the treatment which has been so satisfactorily followed in these severe cases would not give even better results if applied in the earliest stages of cancer of the breast, or at least to employ this method in conjunction with operations for the removal of the glands.

While there have been some apparently striking successes after operations and treatment with thyroid, as suggested by Beatson, it must not be forgotten that untreated cancers are sometimes arrested in their growth and occasionally undergo spontaneous resolution. Aside from this it is very probable that many failures are never reported. E. Percy Patton[2] reports absolute failure in two severe cases. In both cases the growths were associated with either pregnancy or lactation. In one case, after oöphorectomy, 5 grains (0.30 gramme) of thyroid, three times a day, seemed to induce restlessness and insomnia, and was discontinued after three weeks. In the other case no thyroid was administered.

Ulmarene. Ulmarene is a rose-yellow refractive liquid containing 75 per cent. of salicylic ether, and is insoluble in water, but freely soluble in alcohol, ether, or chloroform. The recent investigations of Bordet and Chevalier[3] led them to believe that by reason of the fact that it contains large quantities of the salicylate, and is unirritating to

[1] British Medical Journal, October 19, 1901.
[2] Ibid., March 1, 1901.
[3] La Médecine Moderne, August 15, 1902.

the stomach, it will prove of much value in *rheumatism* when full doses **of salicylates** are required. It may be administered in doses of from 15 **to 75 minims**, three times a day. The most suitable method of admin**istering** it is in capsules, but if desired it may be made into an emulsion **or given** in some alcoholic liquid.

℞.—Ulmarene . . . . . ʒiv.
Pone in capsulas No. xxiv.
Sig.—One to four capsules three times a day.

℞.—Ulmarene . . . . . fʒiv.
Tragacanthæ . . . . . q. s.
Syr. zingiberis . . . . . fʒij.
Aquæ menth. viridis . . . . . q. s. ad. fʒviij.
M. Sig.—Tablespoonful in water three times a day.

℞.—Ulmarene . . . . . fʒiv.
Elix. aromat. . . . . fʒviij
M. Sig.—Two to four teaspoonfuls in water three times a day.

Urea. One of the most enthusiastic advocates of the use of urea in *tuberculosis* is Henry Harper, who believes that it exerts a specific action on the disease, and in an interesting paper[1] discusses the value of the remedy, and reports seven cases of tuberculosis where the good effects of the drug were noticed. The urea which he employs is a synthetic product, and he asks the physiologist and therapeutist to decide if urea obtained from animals would differ in its action from that produced by synthesis. The first case reported was that of a married woman, aged twenty-nine years, who came under his care July, 1901. She was pregnant, and complained much of anorexia, pain, and sickness after the ingestion of food. She had lost about twenty-one pounds in weight, and when lying down had marked dyspnœa. In addition to a severe cough she had several attacks of hæmoptysis, and the sputum was found to be loaded with tubercle bacilli. Night-sweats which she had noticed for three weeks had weakened and depressed her. Examination of the thorax showed advanced tuberculosis, especially noticeable at the base of the left lung. Treatment of urea was instituted, starting with 2-grain doses, three times a day, and increased 10 grains every week until 55-grain doses were reached and maintained for some time. Before the treatment was begun, urea in the urine was about 1 per cent. Examination of the urine several times after urea treatment was begun showed there was no increase, and sometimes it was less, being 0.8 per cent. The cough and general condition improved rapidly, and there was a gain of twelve pounds in weight. The patient considered herself cured, as her cough completely subsided. Harper

[1] Lancet, December 17, 1901.

believes the favorable results in this case were due, to a certain extent, to the pregnancy, and that the base of the lung was involved, instead, as is usually the case, of the apices. She received in all about 27 ounces of urea.

The second case was a woman, aged twenty-two years, who had a tubercular history, her father having died from phthisis. She was ill about four months before submitting herself to his care. There was loss in weight, languor, her sputum contained bacilli, and besides her malnutrition, râles could be heard at the right apex of the lung. The patient was put on urea at once in increasing doses until 50-grain doses, three times a day, were reached. Besides the medicine the regular routine treatment, such as food, exercise, etc., was instituted. After one month of treatment her cough disappeared and the sputum was free from tubercle bacilli, and she gained seven pounds in weight. Her total absorption of urea was 30 ounces and 1 drachm. His third case was a man, aged twenty-five years. An examination revealed a marked pleurisy of the left side, with pulmonary tuberculosis. The cough was severe and the sputum scanty. There was considerable fever and loss in weight. Urea was given until 60 grains were taken daily. Within a month marked improvement was noticeable, and after two months nearly all the evidences of pulmonary trouble had disappeared. The patient had gained fourteen pounds in weight. Dyspnœa disappeared entirely. He consumed about 22 ounces of urea. The fourth case occurred in a boy, aged twenty-two months, having enlarged glands in the neck, and round, hard abdomen, a temperature of about 101° F., and occasional attacks of diarrhœa. The patient was placed upon 4-grain doses of urea flavored with glycerin and peppermint, three times a day. This dose was progressively increased to 10 grains. After a month's treatment the child gained five pounds, the glands had disappeared, and his abdomen was normal. Harper states that in this particular case urea acted like a stimulant and vitalizer, imparting spirit and vigor to the little patient almost immediately. This child received in all about 3 ounces and 2 drachms of urea. On April 7, 1901, a married man, aged thirty years, suffering with tubercular glands, came under his care. For seven years he had enlarged glands in the left side of his neck, and had been receiving medical attention for four years. His family history showed a tubercular diathesis, his father having died of the disease. His whole appearance denoted this tendency; his weight being only one hundred and twenty-eight pounds. This patient was put on urea in increasing doses until 60 grains were taken, three times a day. The enlarged glands disappeared and the weight increased one and one-half stones, and it seemed that here urea acted like a specific upon the tuberculous glands. The sixth case was

a woman, aged twenty-six years, who came under Dr. Harper's observation six and one-half years ago. Two years before she came to him she was suddenly taken ill with acute tuberculosis. Her right lung was tuberculous with a marked cavity at the apex. The sputum teemed with tubercle bacilli. She was treated for several years with the usual methods; that is, receiving abundant nutritious food, cod-liver oil, iron, etc. This patient, who was a great meat eater, improved every year slowly. Recently her right lung showed the invasion of the tubercle bacilli. On June 15, 1901, urea was administered with favorable results; her cough and expectoration disappeared, and after having consumed 38½ ounces of urea she gained ten pounds in weight. The seventh case came under his care about ten years ago, when the patient was twenty years of age. When eighteen months old she had tuberculosis of the spine, and at eight years of age lupus developed on both cheeks, gradually attacking the nose. With the ordinary treatment no improvement was noticed, and it took eight years for the ulcerations about the cheeks and nose to heal. On July 17, 1901, urea was given internally, healing began rapidly, and the patient soon increased ten pounds in weight.

Harper believes the most suitable cases for the administration of urea are those with circumscribed pulmonary tuberculosis of the lung, in which the sputum exhibits an abundance of bacilli and only a limited number of cocci; enlarged tuberculous glands situated on any part of the body; tuberculous pleurisy, tuberculous laryngitis, lupus, tuberculosis of the peritoneum with fluid in the peritoneal cavity, hydrocephalus in children, and tabes mesenterica.

Unsuitable cases are those in which cocci predominate and the tubercle bacilli exhibit a short, stumpy appearance (the typical Koch's bacillus being scanty); acute miliary tuberculosis with high temperature (103° F. or over), and when the patient has a temperature over 101° F. No ill-effects were ever noticed by him in giving urea, although as much as 70 grains, three times a day, has been administered, which is one-half the total quantity of urea excreted by the average healthy person. In the *Therapeutic Gazette*, December 15, 1894, Dr. Samuel G. Dixon suggested the use of the nitrogenous catabolic compounds as remedies against tuberculosis, and reported a case of lupus in which he administered urea, with beneficial results.

Urotropin. With a knowledge of the fact that when administered internally urotropin decomposes into ammonia and formaldehyde, Mayer[1] was led to employ this substance for the purpose of neutralizing the *b*-oxybutyric acid in the blood of a patient threatened with *diabetic*

[1] Medical Record, March 8, 1902.

coma. He administered 20 grains of urotropin, repeated in two hours, and, as there was much improvement upon the following day, the drug was continued in daily doses of 20 to 60 grains until there was so much irritation of the bladder that it was necessary to discontinue it. It was thought that four threatening attacks were successfully aborted by the use of urotropin, but the diabetes remained unchecked, and the patient died in the fifth attack of coma. As urotropin is only decomposed into its component parts in the kidney, it is probable that only very small quantities of ammonia are absorbed by the renal veins, and it seems that much more good may be accomplished by the intravenous injection of alkaline solutions.

Valyl. Diamethyl-amid of Valerianic Acid. From a study of the various preparations of valerian as found in the shops, Kionka and Liebrecht[1] became convinced that the uncertainty of the action of these preparations depends upon their instability. They were able to derive from fresh valerian a colorless fluid, having a penetrating odor and a burning taste, which was stabile, and upon chemical analysis proved to be dimethyl-amid of valerianic acid.

Clinical application showed that this substance represented the full therapeutic value of valerian. Owing to its disagreeable odor and the burning sensation left in the mouth after its administration in concentrated form they were led to mix this active principle with mutton suet, inclose it in capsules, and found this a convenient method for administration. The doses of the fluid they called valyl is from 1 to 2 grains. They employed it successfully in treating hysteria, neurasthenia, traumatic neurosis, neuralgia, anomalies of menstruation, and nervous symptoms of the menopause.

Veratrum Viride. Last year I called attention to the opinions expressed by a number of prominent American obstetricians regarding the value of veratrum viride in *eclampsia.*

It will be recalled that while there were differences of opinion, the weight of the evidence was favorable to its use under certain circumstances.

During the past year others who mention the drug favorably are A. B. Chase,[2] B. B. Bar,[3] M. W. Van Denberg,[4] A. Lapthorn Smith,[5] and W. E. Parke.[6]

In addition to its powerful vasomotor and cardiac effect Dr. A. Gilardoni, of the University of Pavia, has recently shown by experiments upon animals and human beings that the drug may be classed

[1] Deutsche med. Wochenschrift, December 5, 1901.
[2] Therapeutic Gazette, October 15, 1901.
[3] Ibid., February 15, 1902.
[4] American Medicine, February 22, 1902.
[5] Montreal Medical Journal, January, 1902.
[6] Medical News, May 24, 1902.

as a true diuretic, that is, that it increases the elimination of the solid as well as the liquid constituents of the urine.

In Ward's case of eclampsia the remedy not only acted as an antispasmodic and diuretic, but also as a powerful diaphoretic. Taking, then, into consideration the antispasmodic, diuretic, and diaphoretic action of veratrum viride, we can readily understand how, in properly selected cases, it can be of very great value.

Vioform. Iodo-chloroxy-chinolin. Few of the compounds containing iodine, used as substitutes for iodoform, have been satisfactory. No doubt, the reason for this lies in the fact that, while they may act as efficient drying powders, they do not act as favorably upon syphilitic or tubercular lesions as does iodoform.

About a year ago Dr. Krecke[1] called the attention of the profession to vioform, an iodine compound originally introduced by Savel, of Berne, which he claimed to be as effective as iodoform upon syphilitic, tubercular, and other sores, and entirely free from any disagreeable odor. As suppuration is likely to follow injections of this substance into tubercular joints, he does not recommend its use in this manner. From studies made upon guinea-pigs, Dr. James E. Blake[2] finds that in consequence of its insolubility and stability, neither the powder nor its decomposition products are absorbed in any appreciable quantities when locally applied where escape of the secretion is possible. When, however, it is injected into cavities where it cannot readily escape it produces intoxication of considerable severity that may continue for weeks, owing to its slow absorption. Because of its higher antiseptic potency and its freedom from odor, Blake considers vioform superior to iodoform for all purposes except that of injection. Chemically, vioform is iodo-chloroxy-chinolin. It is a yellowish powder, neutral in reaction, odorless, and insoluble.

Wright's Prophylactic Vaccine against Typhoid. It will be remembered that this is not a serum, but a fluid containing dead bacilli and the specific toxin which has been elaborated by living bacilli grown upon peptone bouillon. The vaccine is not employed as a curative agent in the presence of the disease, but is used exclusively as a preventive; in fact, if used during an attack of typhoid, patients are made extremely ill. In a recent series of experiments carried out by Wright,[3] it was shown that if very large doses of the vaccine are injected the resistance to infection by typhoid is almost immediately lowered, and is probably not followed by the protective influence of the fluid. If moderate doses are employed the resistance of the individual

[1] Münchener med. Wochenschrift, 1901, No. 33.
[2] Brooklyn Medical Journal, October, 1902.
[3] Lancet, September 14, 1901.

is also temporarily lowered for a period of about three weeks, but this is followed by an increased resistance on the part of the subject to typhoid infection. If small doses of the vaccine are used the protective influence of the remedy is immediate, but does not persist as long as when medium doses are given. The inference to be drawn from these experiments is that in the presence of an epidemic of the disease smaller doses repeated once are much safer and better than larger ones, but if persons are not likely to be exposed to the infection of typhoid for a period of three or four weeks, or when it is not practicable to revaccinate them, the moderately large doses should be used. It has been extensively employed upon the English troops, and the results reported by A. E. Wright, the originator, from time to time. Two articles have recently appeared which apparently prove the value of the vaccine. An epidemic of typhoid fever broke out in the Richmond Asylum for the Insane (Dublin) on August 7, 1900, and continued until the close of December. On September 6th inoculation of the insane was begun, so that by November 30th, 511 persons had been injected. None of the nursing staff, consisting of 114, nor inmates beyond the age of fifty-five years were operated upon. The quantity of vaccine used in each inoculation was 0.75 c.c. The constitutional symptoms following the injections were said to have been light in all cases. The temperature rose in all cases, usually to 101°F. to 102° F., and in some cases to 103° F. to 104° F., but after a few days fell to the normal. Headaches, vomiting, loss of appetite, diarrhœa, prostration, with stiffness of the muscles of the back, and pain and swelling at the seat of the injection were some of the disturbances produced by the injection, but the patients were, as a rule, able to be up and about on the third or fourth day. At the beginning of the inoculations it was estimated that 655 persons in the institution were exposed to the infection; 541 of these were insane inmates, and 114 were nurses. As stated, 511 patients were inoculated, 7 of the inoculated and 29 uninoculated persons subsequently developed typhoid fever. From the history given, 2 at least of these were suffering with the disease at the time of the inoculation. Owing to the constitutional disturbances produced by the injections, it was necessary to inoculate the inmates in groups. It was estimated that during the epidemic there was a daily average of 298 uninoculated and 339 inoculated persons, including inmates and nurses, exposed to typhoid infection. The results, which are very favorable to the use of the vaccine, are given below:

	Average of strength.	Number of cases.	Number of deaths.	Per cent. of cases.	Per cent. of deaths.
Uninoculated . .	298	30	4	10.1	1.3
Inoculated . . .	339	5	1	1.5	0.8

The same writer gives another statistical report (*The Lancet*, April 5, 1902) furnished him by Lieut. J. W. West, bearing upon the results obtained from the use of the vaccine upon the soldiers of the Fifth Battalion Manchester Regiment, serving in South Africa. The total strength of the battalion consisted of 747 men and officers, 200 of whom were inoculated. Of the 547 uninoculated there were 21 (4.2 per cent.) cases of typhoid fever, with 7 (1.3 per cent.) deaths, while of the 200 inoculated there were 3 (1.15 per cent.) cases of typhoid with no deaths. It is stated that in the three inoculated men who contracted the fever the disease was of a very mild type, while some of the uninoculated cases were not yet out of danger at the time of the report.

Yeast. Numerous authors have, from time to time, testified to the value of brewer's yeast as a therapeutic agent, but the exact constituent to which it owes its value and the method of its action is still in doubt.

In addition to a proteid nuclein and nucleinic acid, the following ferments have been separated from it: Invertin, which transforms cane sugar into dextrose and levulose; zymase, a monosaccharid splitting ferment; endotrypsin, a proteolytic ferment and probably a glycogenic ferment. It is probable that the ferments aid the processes of digestion, and themselves become assimilated and influence bodily metabolism.

Huber attributed the therapeutic value of yeast in certain cases to the power of nuclein and nucleinic acid to produce leucocytosis, McClintock, Novy and Vaughn to the germicidal action of nuclein in the blood, while Bleyer attributed the good effects of yeast in some cases to the vigor imparted by it to the central nervous system. Tournier asserted that brewer's yeast has the power to attract and devour microorganisms.

The effect of yeast upon bacteria has recently been studied by R. Panichi,[1] R. Rapp,[2] and L. Geret.[3]

Panichi found that the addition of yeast to fecal matter diminishes the number of microbic colonies that can be grown in Petri dishes; that fecal matter of subjects to whom yeast is administered shows fewer colonies after than before administration, that it has the property to inhibit the growth of the staphylococcus aureus in culture, and that its administration to animals receiving injections of a culture of staphylococcus aureus alters the effect of the injection or neutralizes it altogether.

R. Rapp and L. Geret believe that the bactericidal action of yeast is

[1] Giornale italiano delle Mal. Ven. e. del. pelle, 1901.
[2] Münchener med. Wochenschrift, September 9, 1902. [3] Ibid., 1906, No. 46.

due to the presence of zymase. Geret, in his experiments, showed that active fermentative yeast causes marked reduction in the number of colonies of an active culture of typhoid bacilli which was added to it. Under certain circumstances the cultures were rendered completely sterile, but if the solution is slightly alkalinized the bactericidal action of the yeast is diminished.

Durand,[1] Paschkis,[2] Rapp,[3] and others during the past year have employed yeast with satisfactory results in treating *furunculosis*. Durand found the remedy of particular value in treating *boils*, *acne*, and other pustular and suppurative skin lesions due to intestinal disorders. He also used it locally with good effects in treating *tonsillitis*, *burns*, and *vaginitis*.

Paschkis found that the therapeutic action of yeast was remarkably effective in some cases of furunculosis and folliculitis, while others proved refractory. He states that if a considerable quantity of sugar is taken by the patient during the yeast treatment, flatulency may become annoying.

Rapp believes that many of the negative reports from the use of yeast in furunculosis are due to inefficient preparations employed. An examination by him of five widely used preparations showed that they vary considerably in the amount of water and number of bacteria as well as in the fermentative, digestive, and bactericidal power.

I. Lardier and Toubet,[4] and Julius Ullman[5] have employed yeast with asserted good effects in the treatment of pulmonary affections. Lardier considers it peculiarly valuable in treating both *acute* and *chronic bronchitis* in the aged. He does not depend upon it to the exclusion of other remedies, but employs dry yeast in doses of two or three teaspoonfuls a day when the disease has begun to recede and the patient begins to expectorate. In such cases the amount of expectoration is distinctly decreased within two or three days, and a cure effected within two or three weeks. In *pneumonia* it seems to have the same effect if employed at the time of defervescence. Ullman found the remedy to be of value not only in bronchitis or bronchopneumonia, but also for diminishing night-sweats, temperature, and general depression in *pulmonary tuberculosis*.

P. Chapelle[6] and W. Albert[7] consider yeast a valuable antiseptic and therapeutic agent in treating *leucorrhœa*, *vaginitis*, and *erosions of the*

[1] Lyon Médicale, February 9, 1902.
[2] Wiener klin. Wochenschrift, July 31, 1902.
[3] Münchener med. Wochenschrift, September 9, 1902.
[4] Semaine Médicale, 1902, No. 30.
[5] American Medicine, October 11, 1902.
[6] Journal de Paris, November 25, 1901.
[7] Centralblatt f. Gynäk., August 16, 1902.

cervix. Chapelle attributes its value to its phagocytic action. Owing to the inconveniences attending the application of ordinary brewer's yeast, he employs the desiccated product known as "cerevisine," which may be made into suppositories by the addition of glycerin and starch, and retained in the vagina by cotton tampons. Albert found yeast of value as a disinfectant within the vagina, to be used prior to operations, and for treating vaginal catarrh.

As a result of experiments upon animals, Carrion and Hallion[1] claim to have discovered that yeast is an energetic antitoxin against the diphtheria toxin, and also acts favorably when applied locally to the false membranes.

In applying yeast treatment, a good, reliable brewer's yeast obtained fresh daily, or some one of the dehydrated preparations which have been tested, should be employed.

[1] Gazette hebdomadaire, April 27, 1902.

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